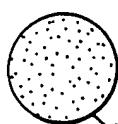


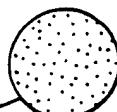
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# FIG. 1



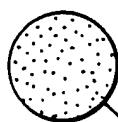
[ SEQ. ID NO: 3]

X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C  
5' 3'

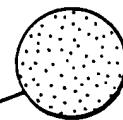


G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X  
3' 5'

[ SEQ. ID NO: 4]



X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C  
G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X



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FIG. 2

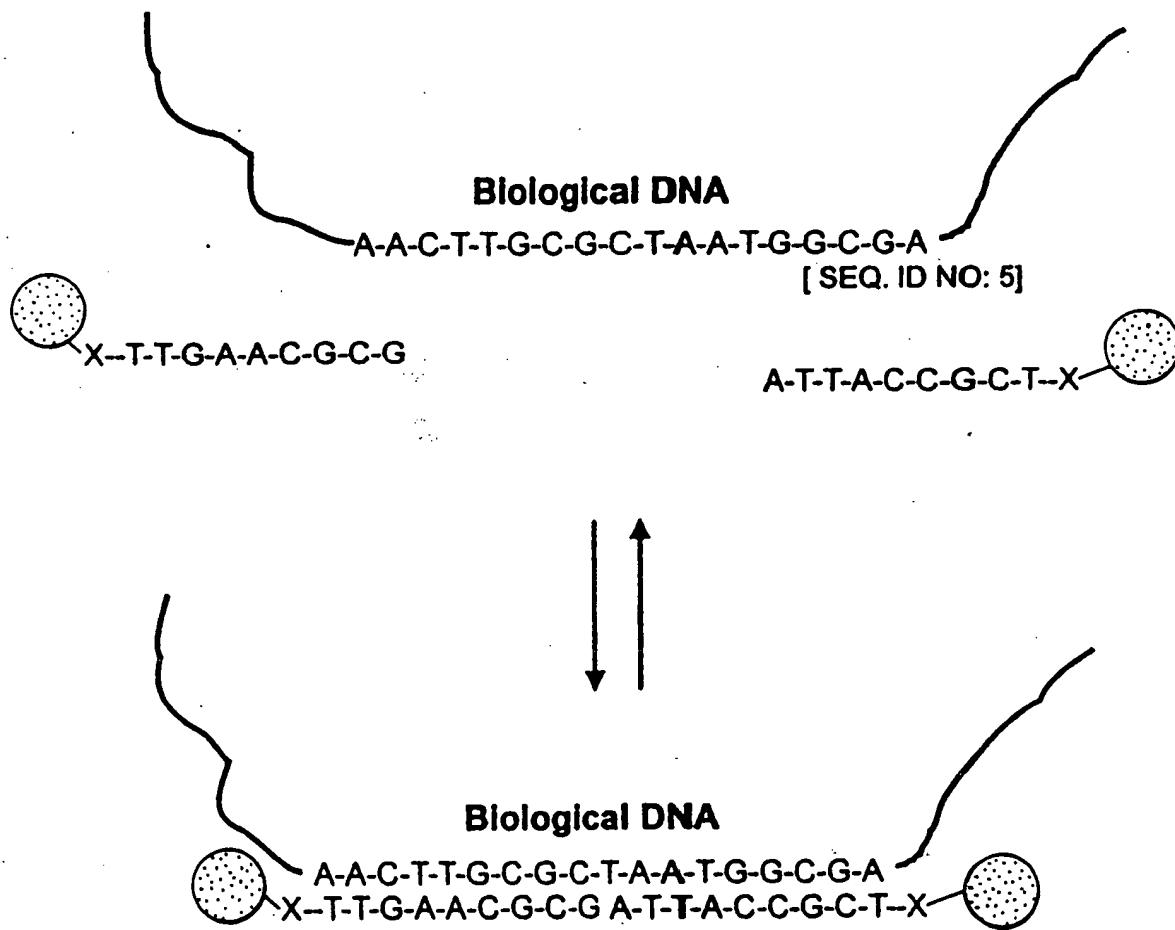
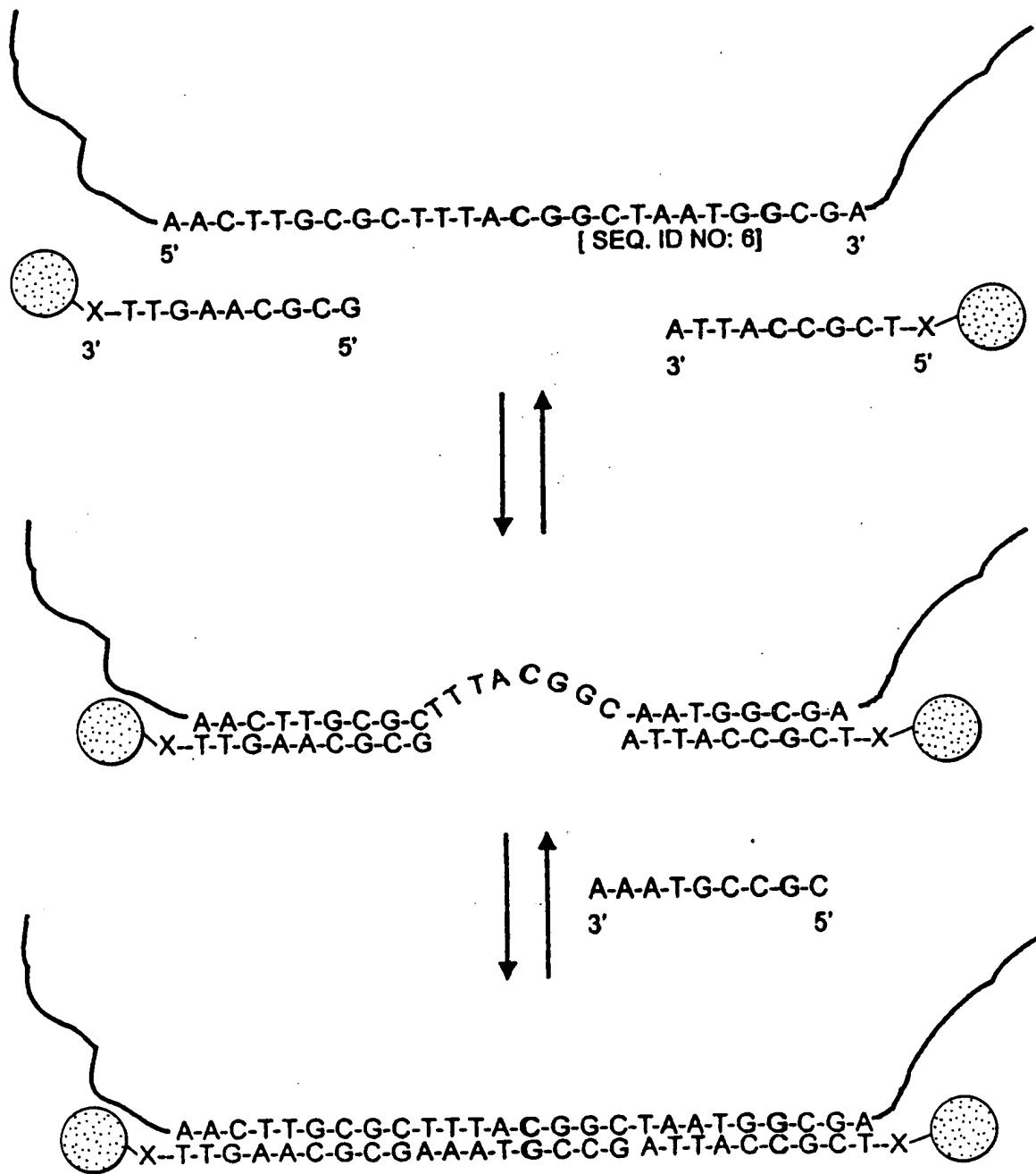


FIG. 3



# FIG. 4

5' A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-T-A-G  
 3' [SEQ. ID NO: 2] →  
 5' A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A  
 [SEQ. ID NO: 1] →

Linking oligonucleotide

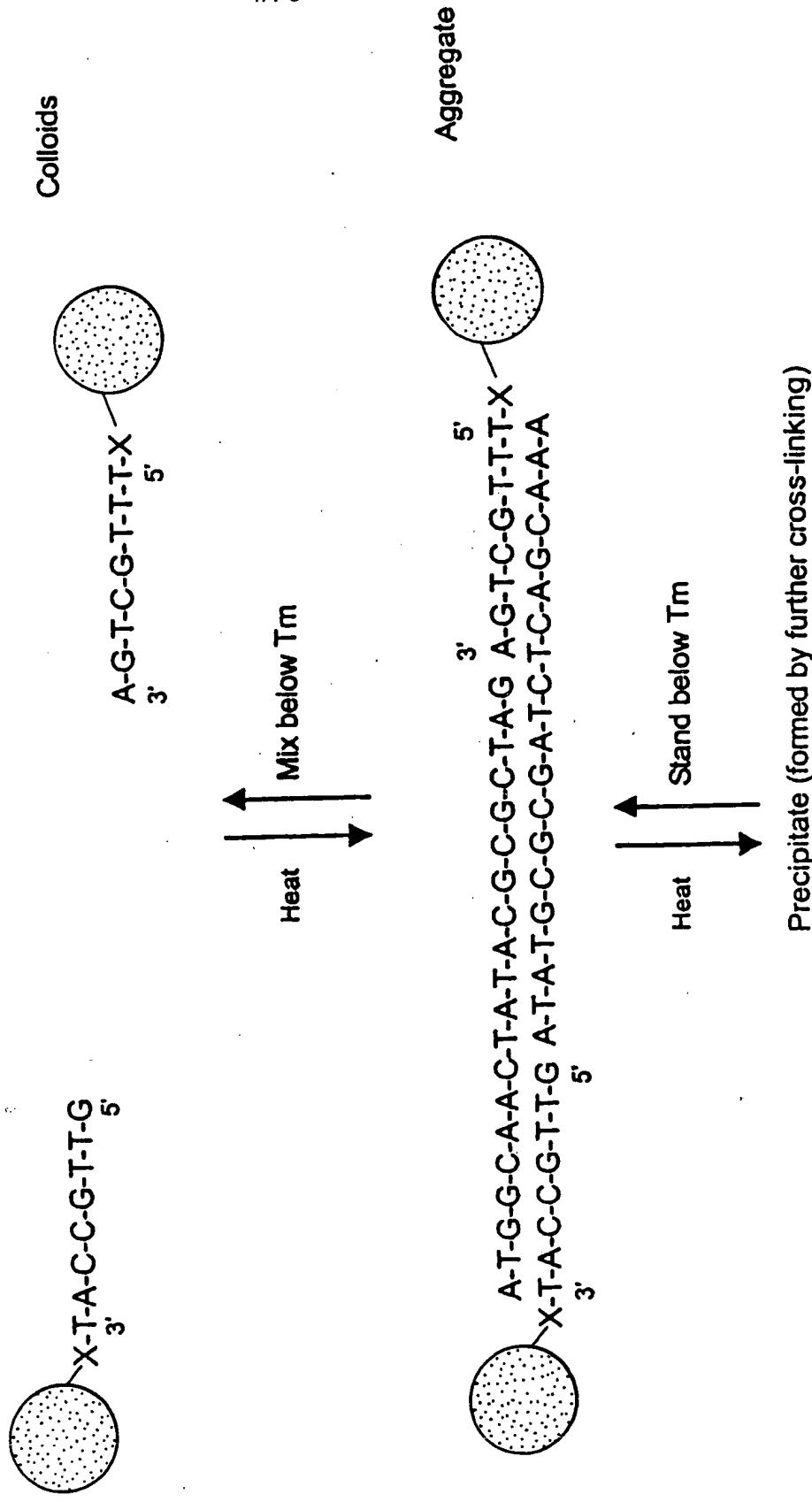
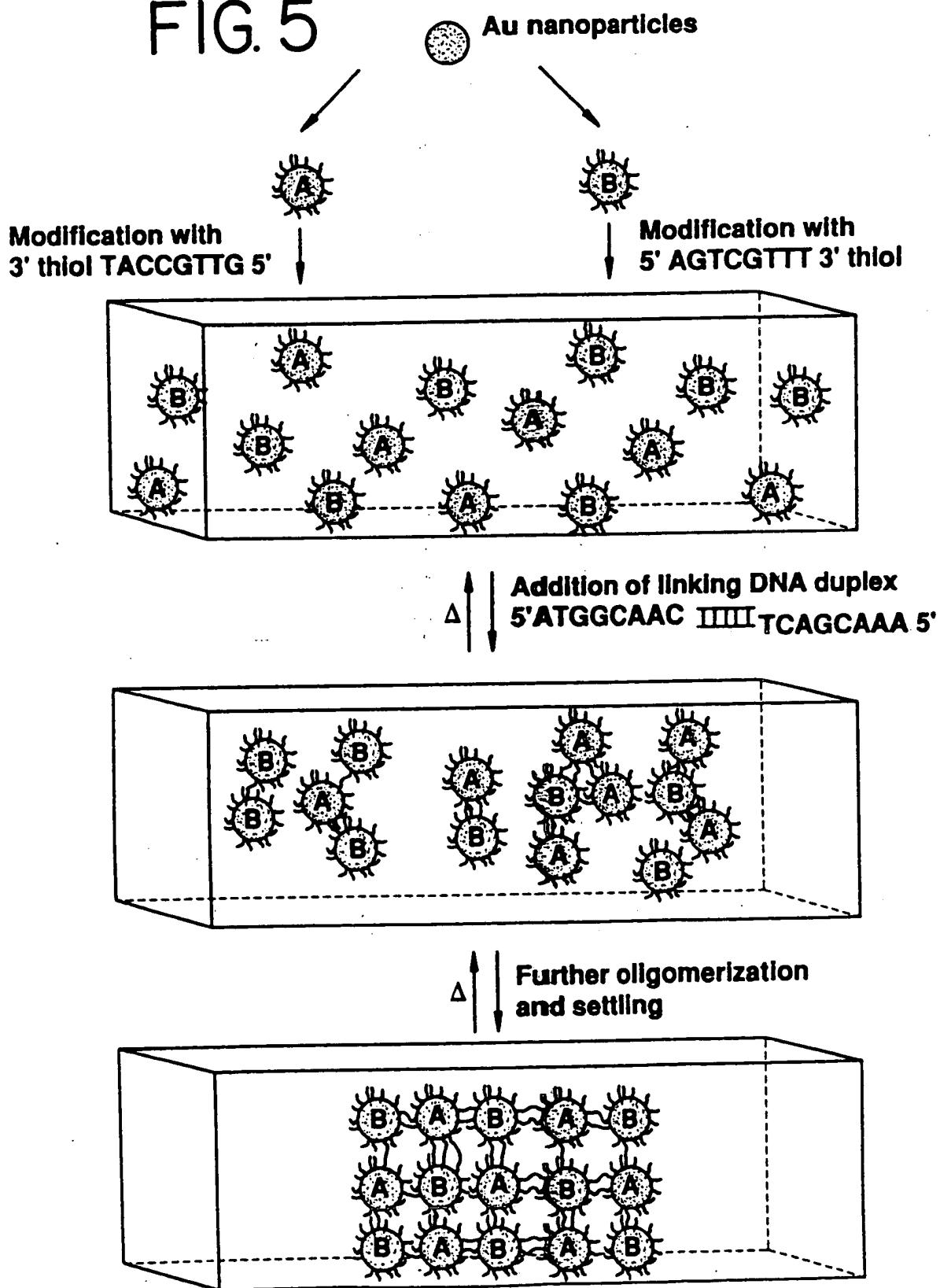


FIG. 5



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**FIG. 6A FIG. 6B FIG. 6C**

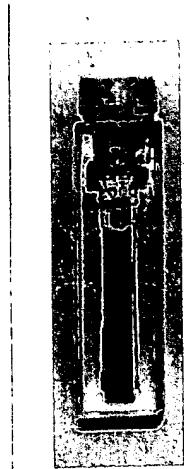
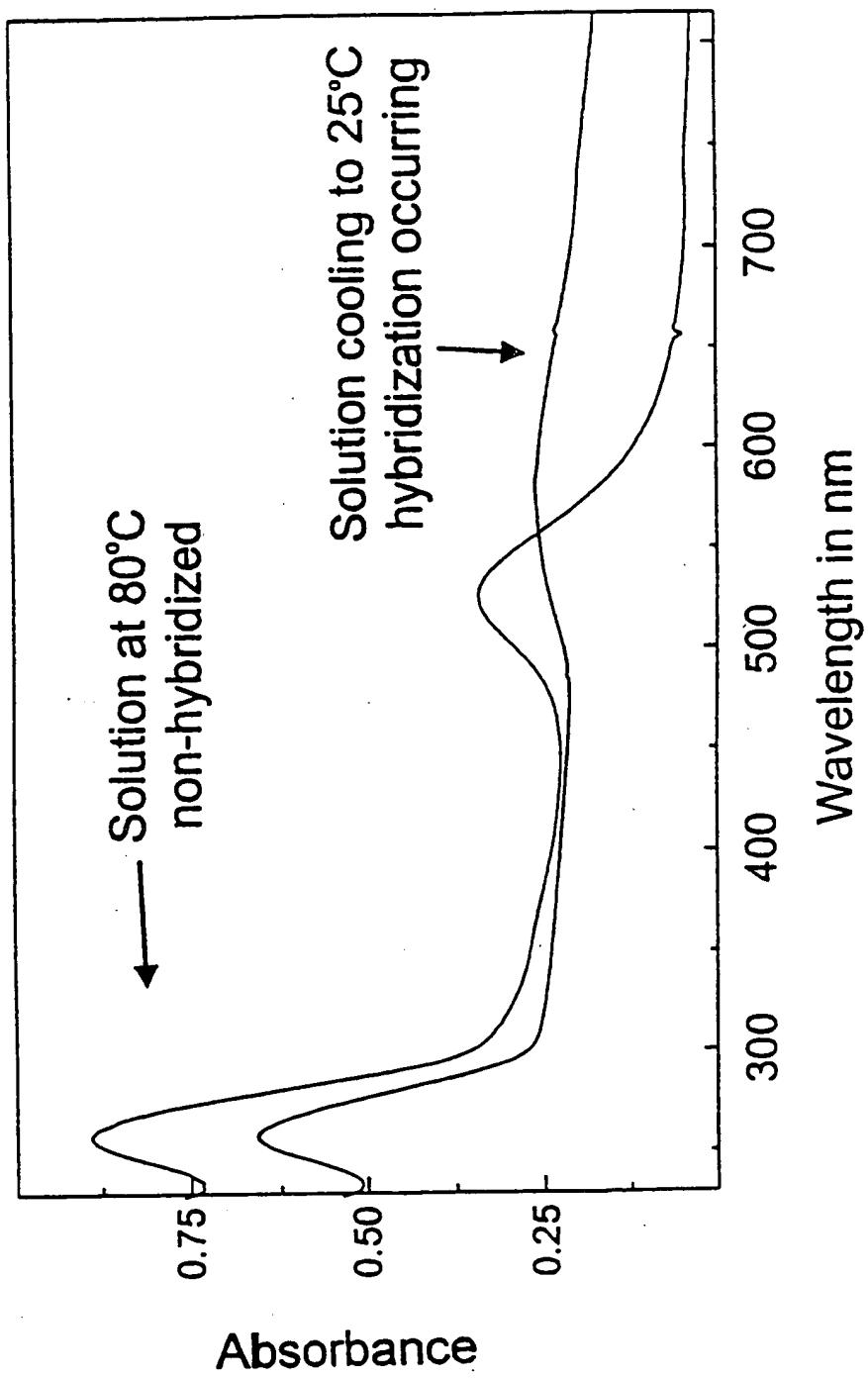
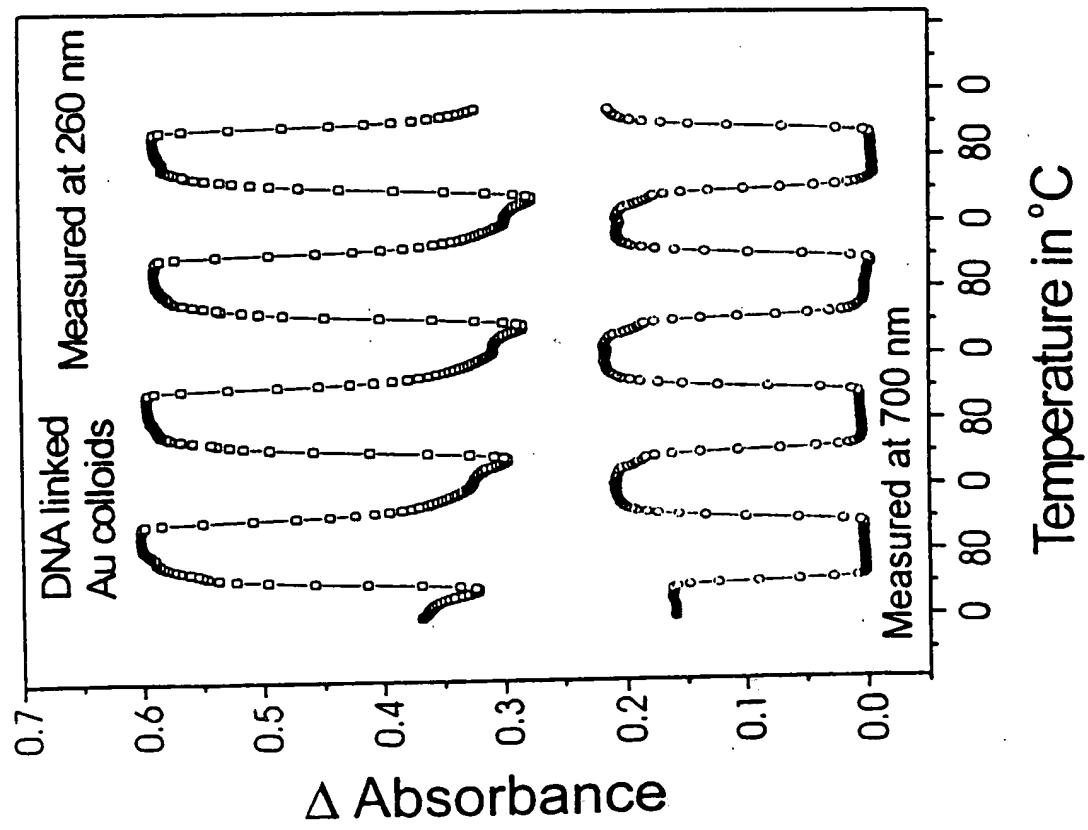


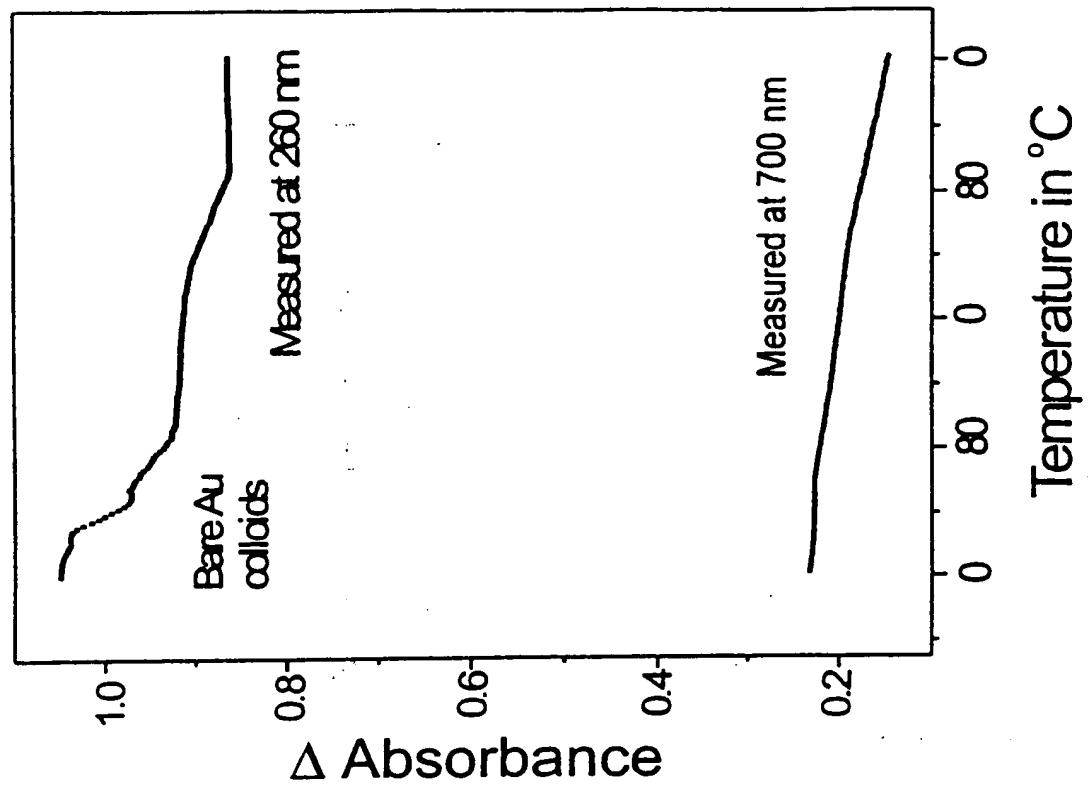
FIG. 7



**FIG. 8A**

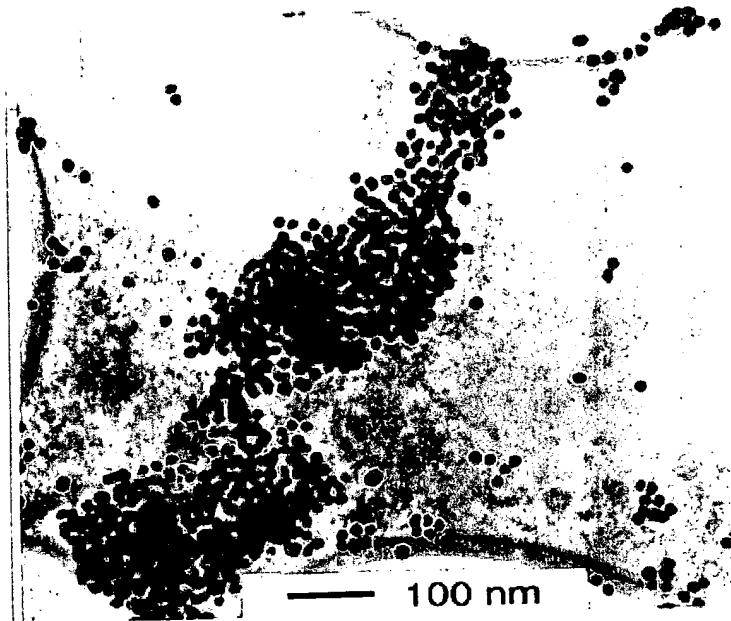


**FIG. 8B**

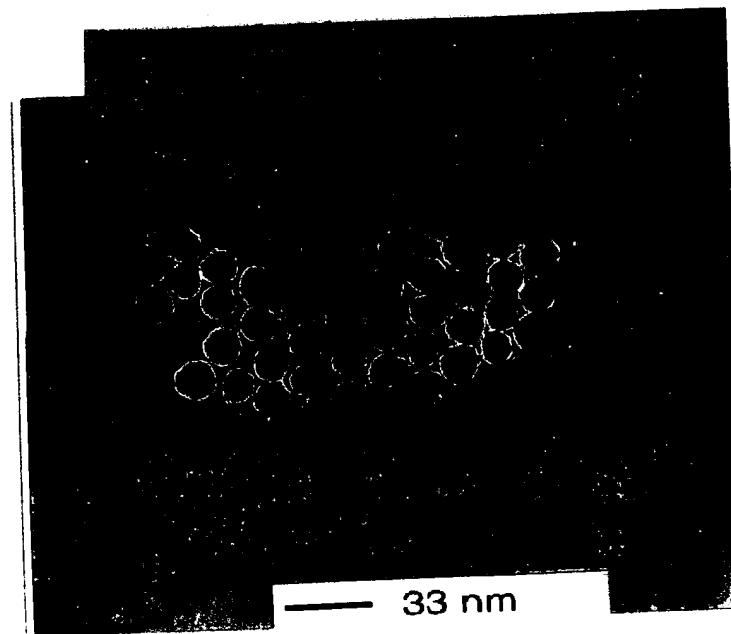


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**FIG. 9A**

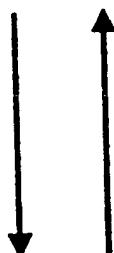
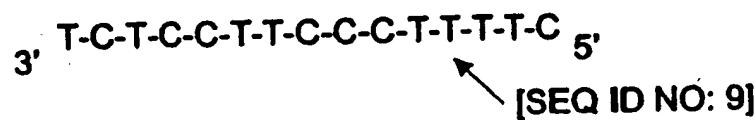
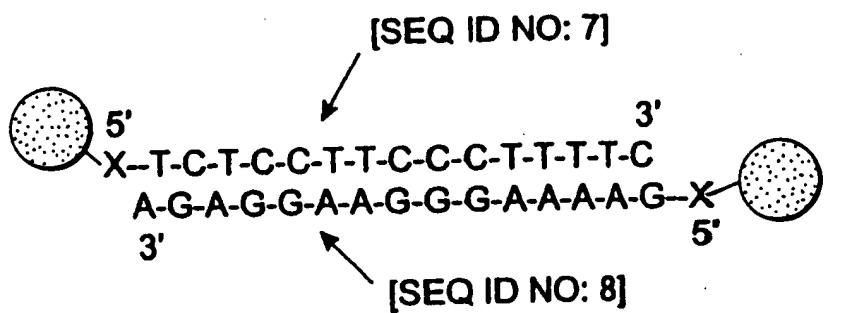


**FIG. 9B**

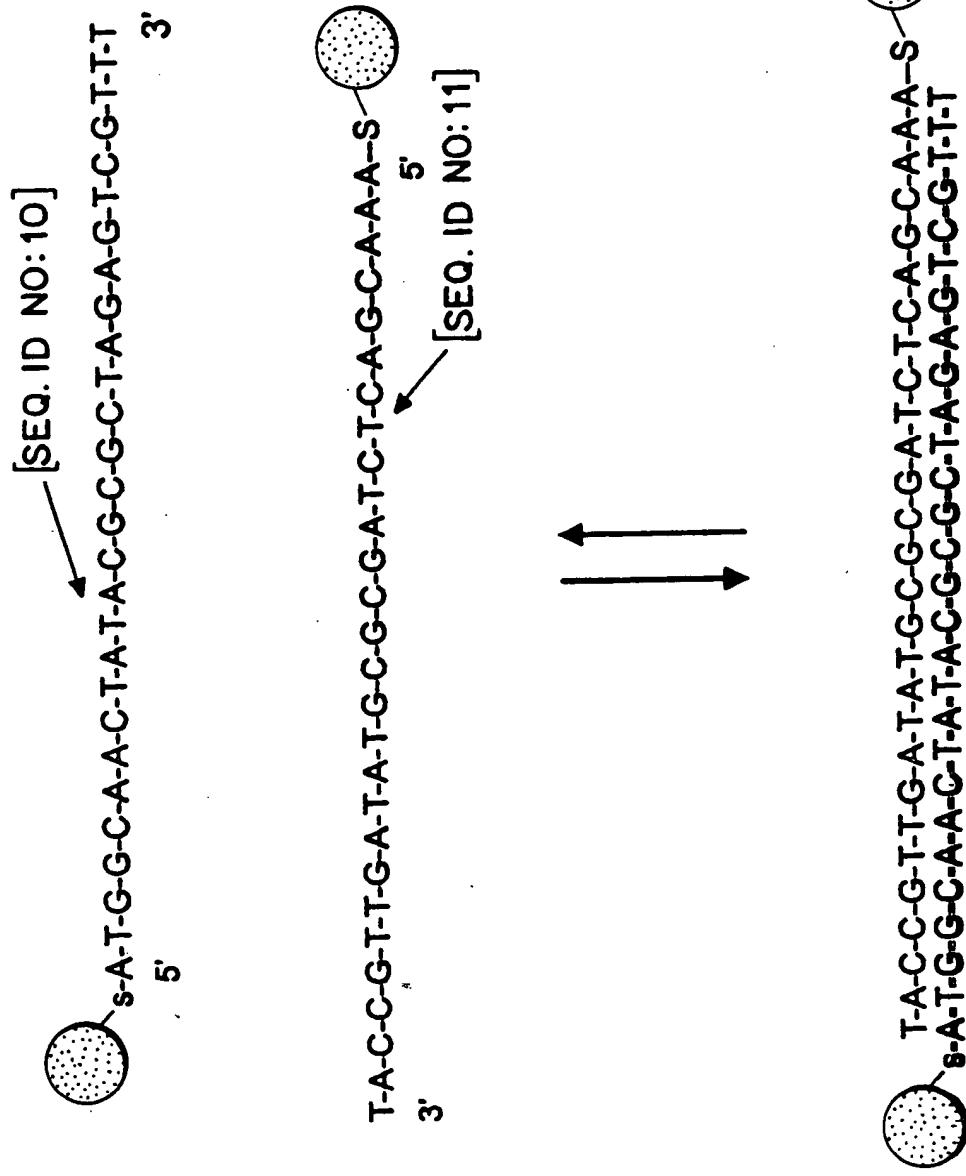


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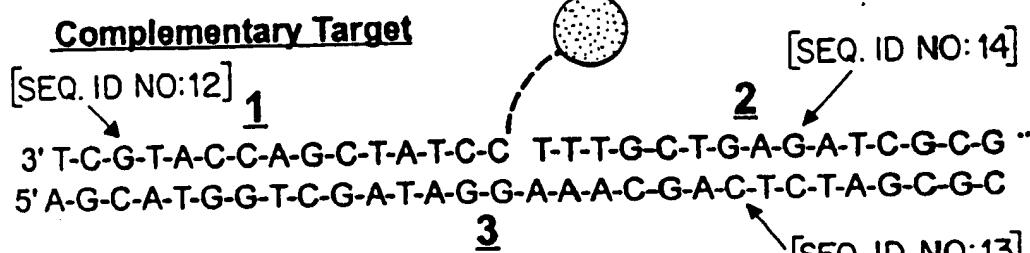
# FIG. 10



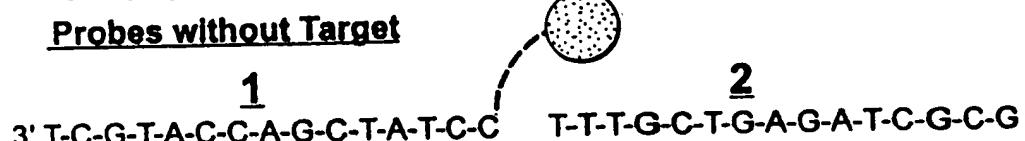
# FIG. II



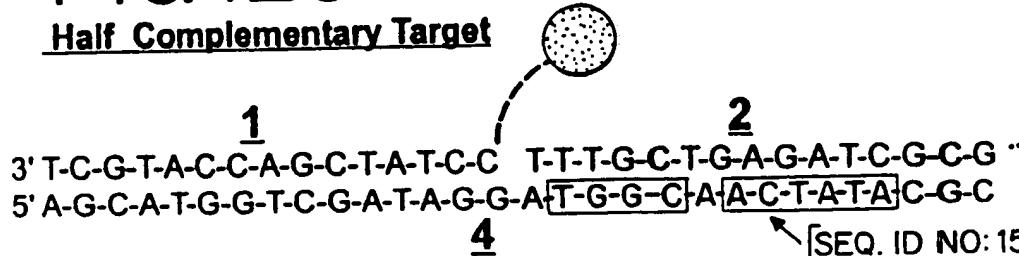
# FIG. I2A



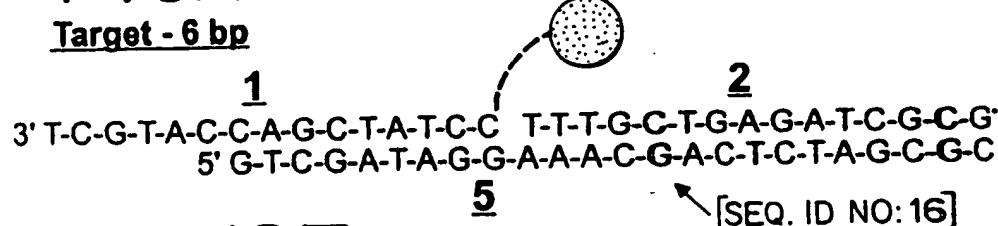
# FIG. I2B



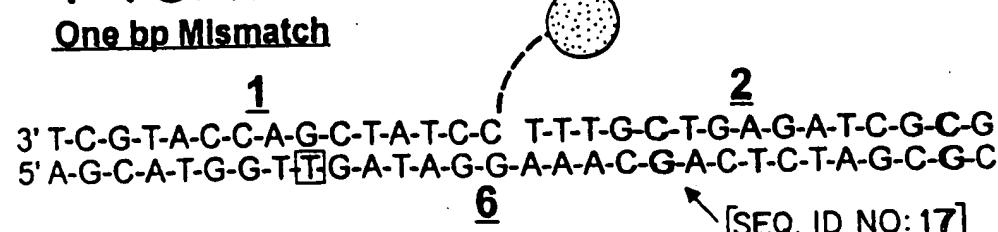
# FIG. I2C



# FIG. I2D



# FIG. I2E



# FIG. I2F

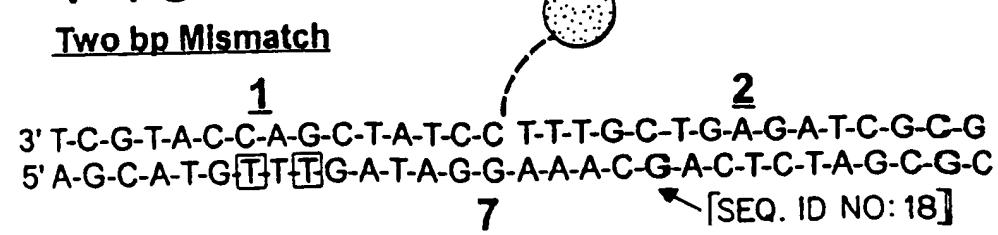
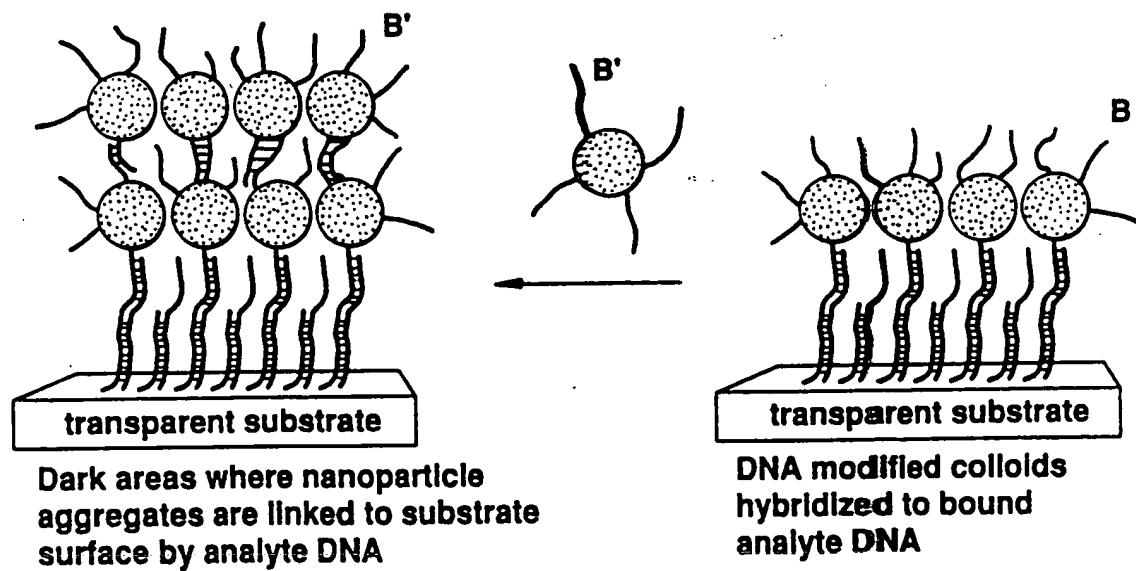
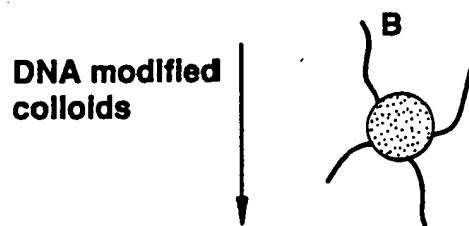
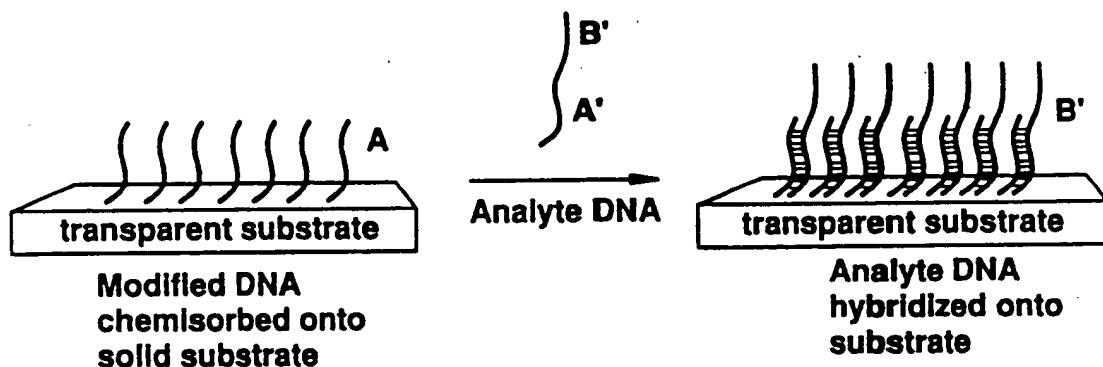


FIG. 13A



**FIG. I3B**

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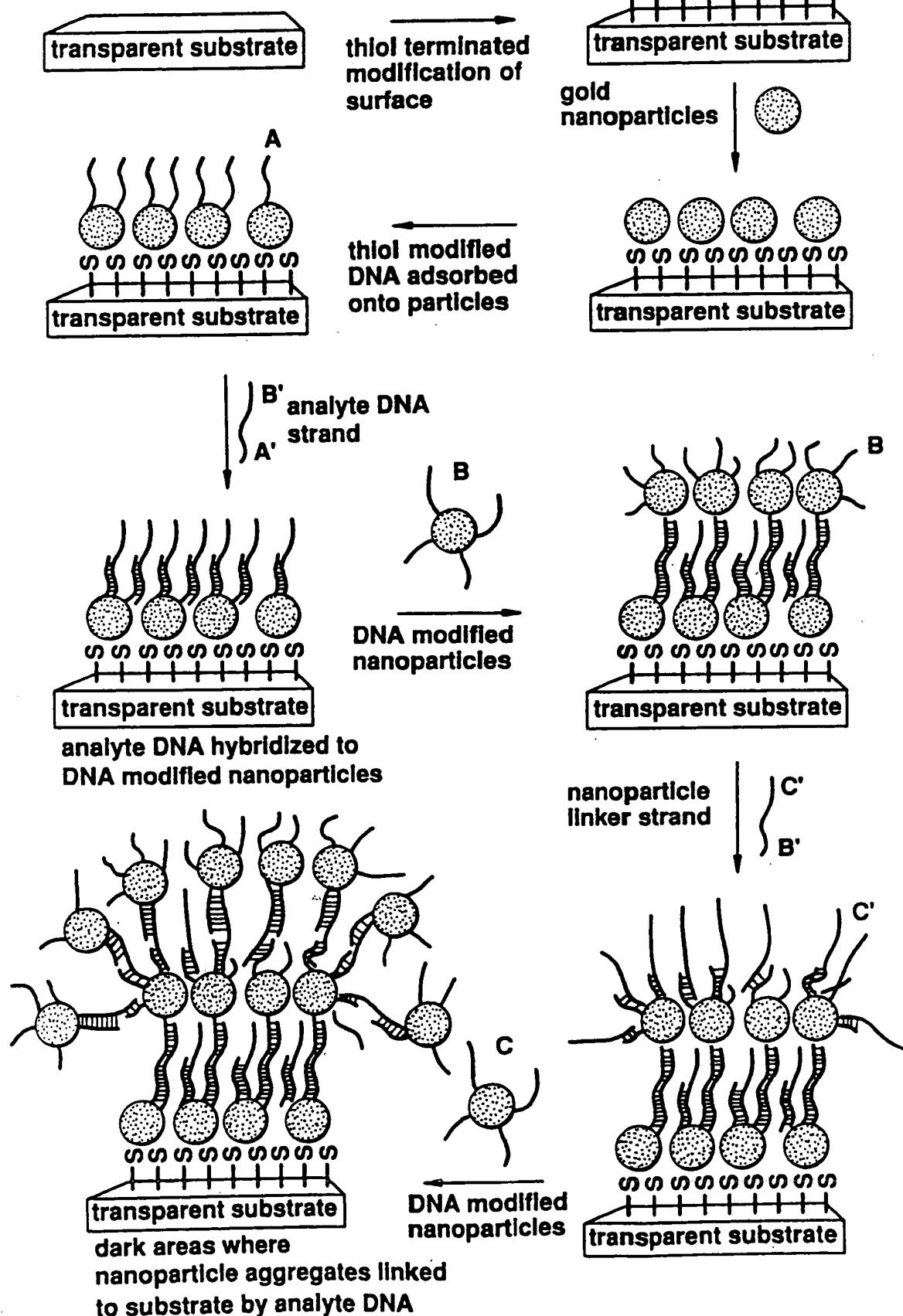


FIG. 14A

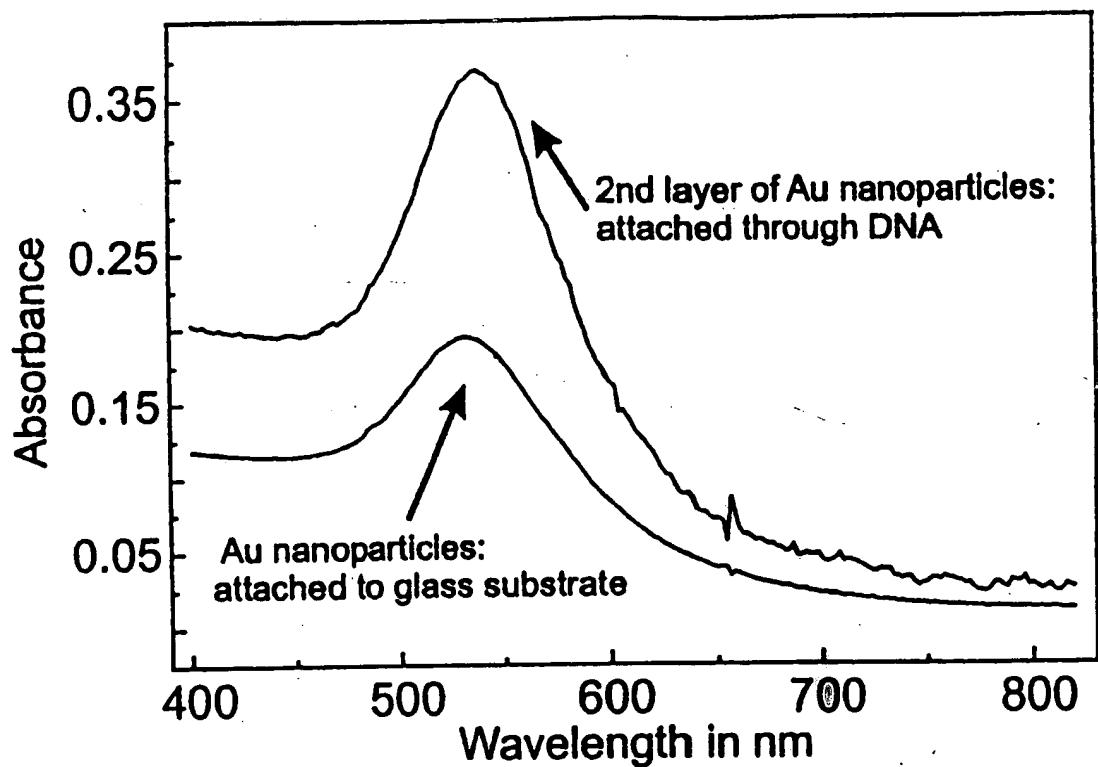
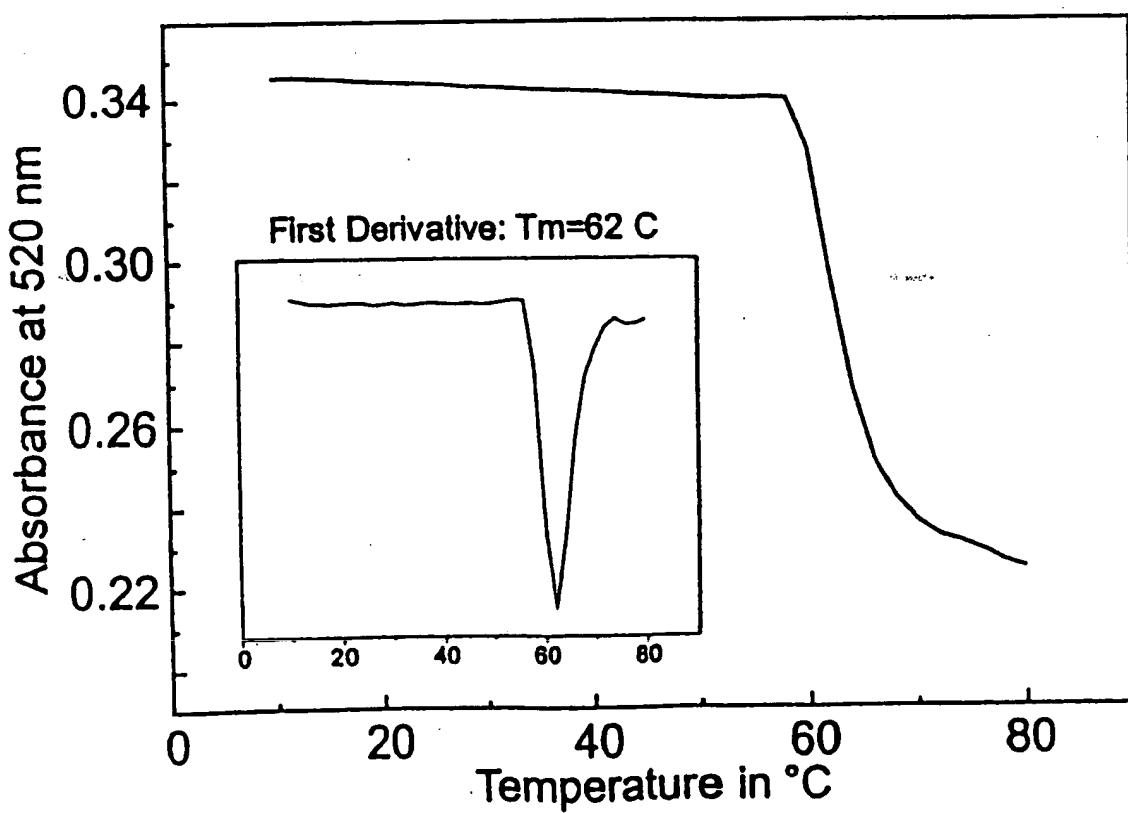


FIG. 14B



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FIG. 15A

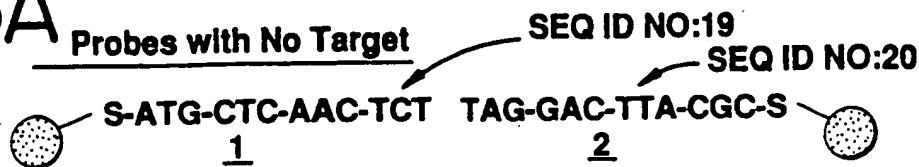


FIG. 15B

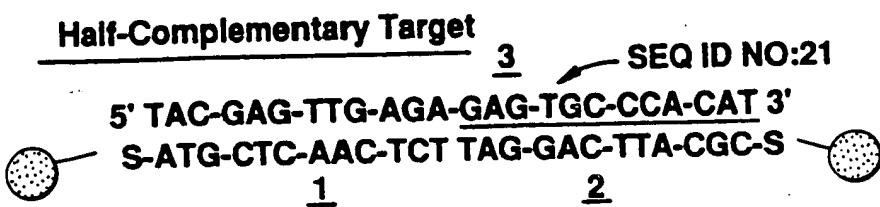


FIG. 15C

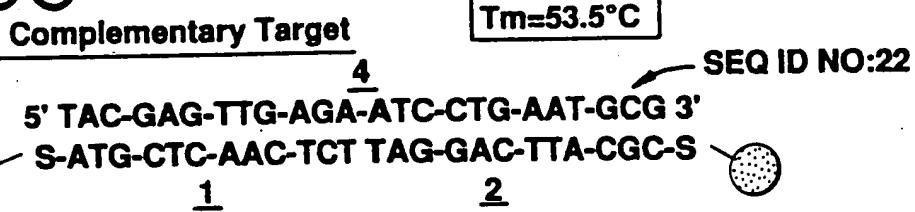


FIG. 15D

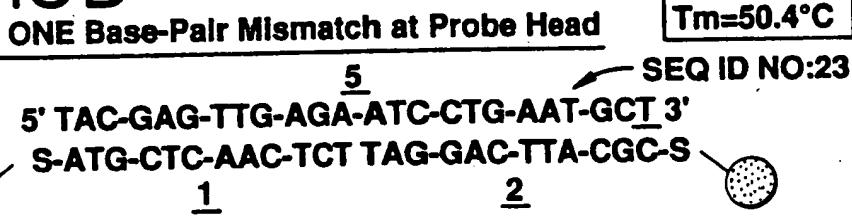


FIG. 15E

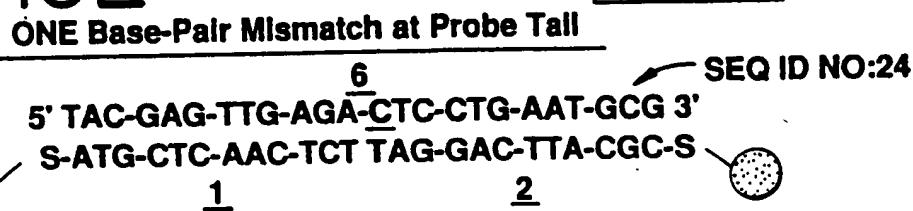


FIG. 15F

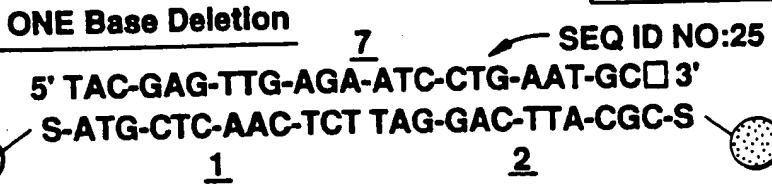
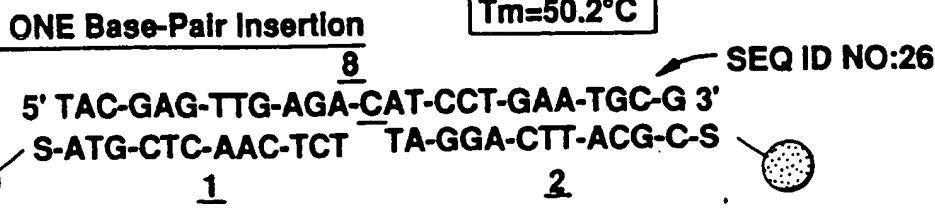


FIG. 15G



## FIG. 16A

### 24 Base Template

5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCG 3'  
—S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S —  
1  
2

## FIG. 16B

### 48 Base Template with Complementary 24 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-ATC-CTG-AAT-GCG 3'  
—S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT TAG-GAC-TTA-CGC-S —  
1  
2

## FIG. 16C

### 72 Base Template with Complementary 48 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-TAT-ATT-GGA-CGC-TTT-ACG-AAC-ATC-CTG-AAT-GCG 3'  
—S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT-ATA-TAA-AAA-TGC-CTG-TTG TAG-GAC-TTA-CGC-S —  
1  
2

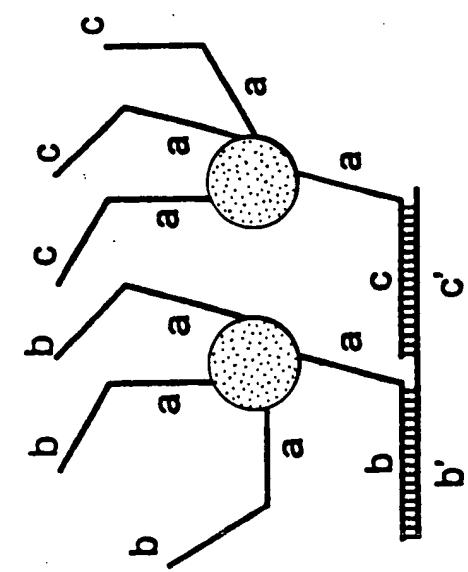
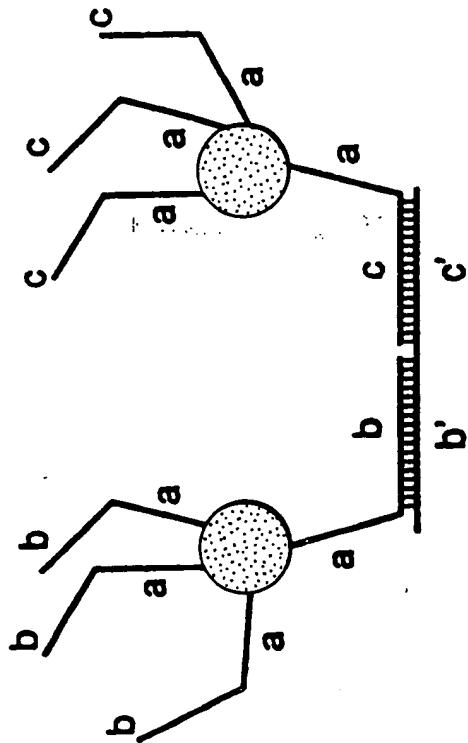
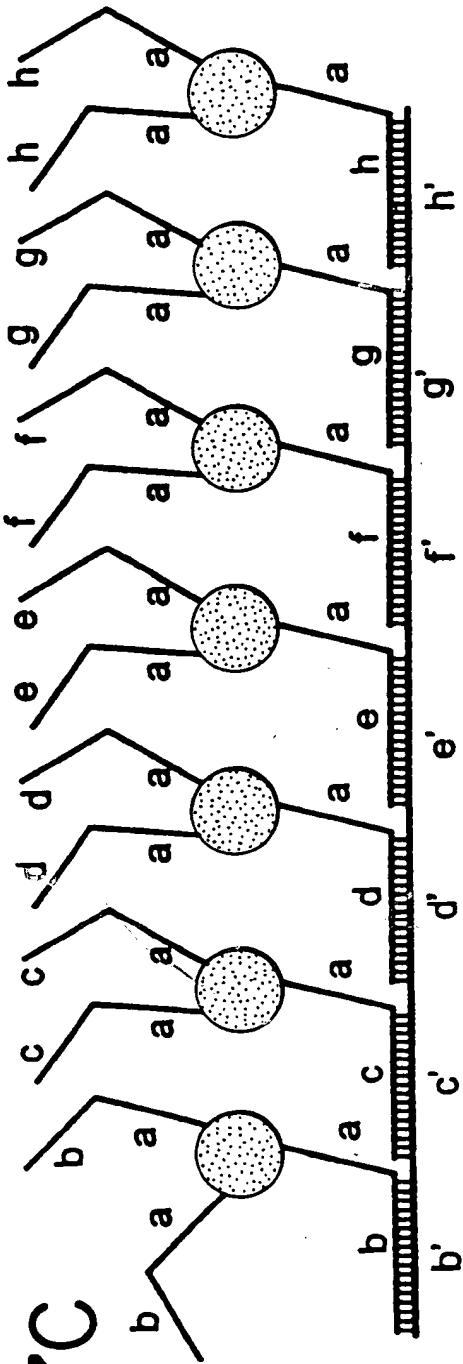
**FIG. 17B****FIG. 17C**

FIG. 17D

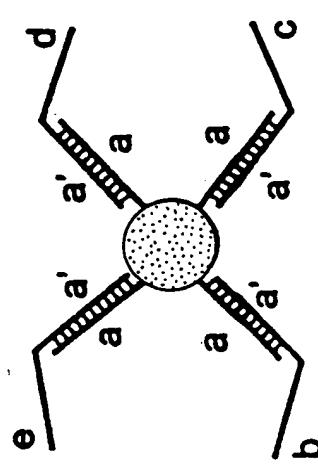
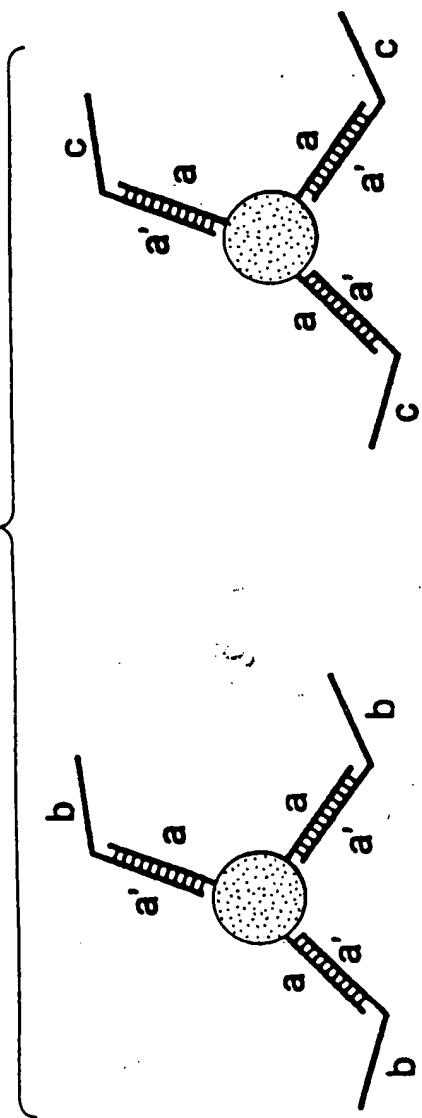
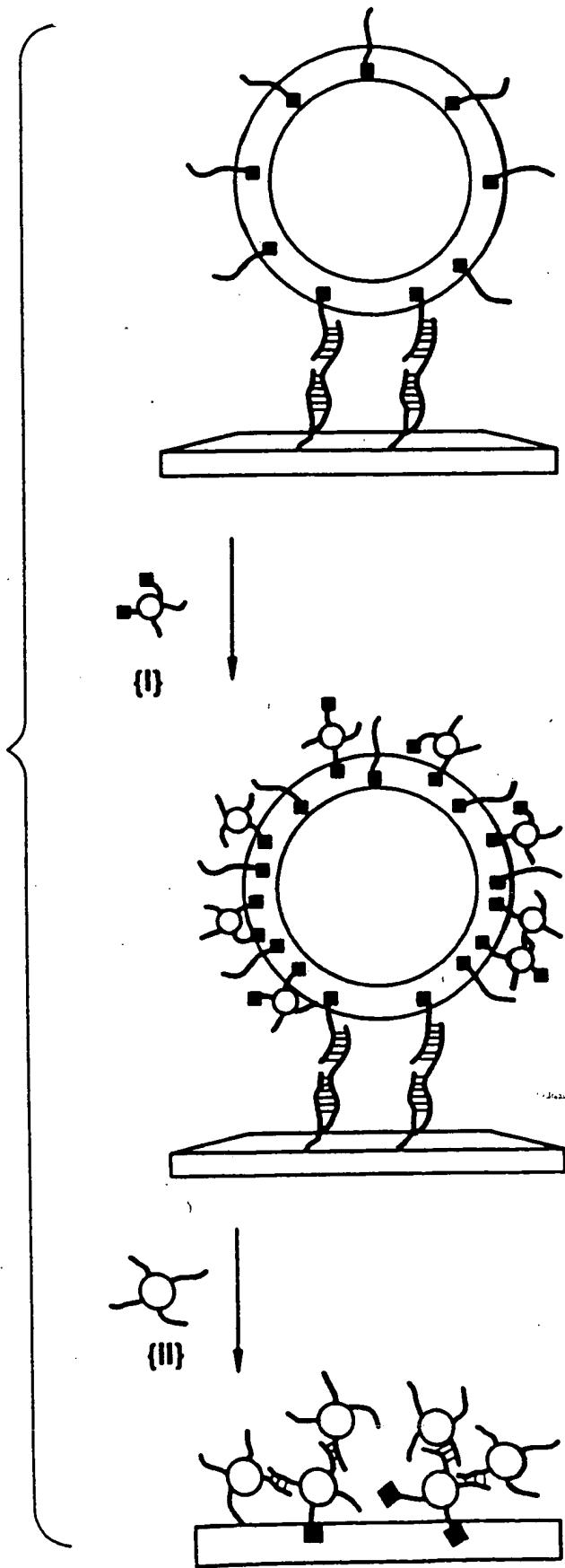


FIG. 17E

FIG. 18

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FIG. 19A

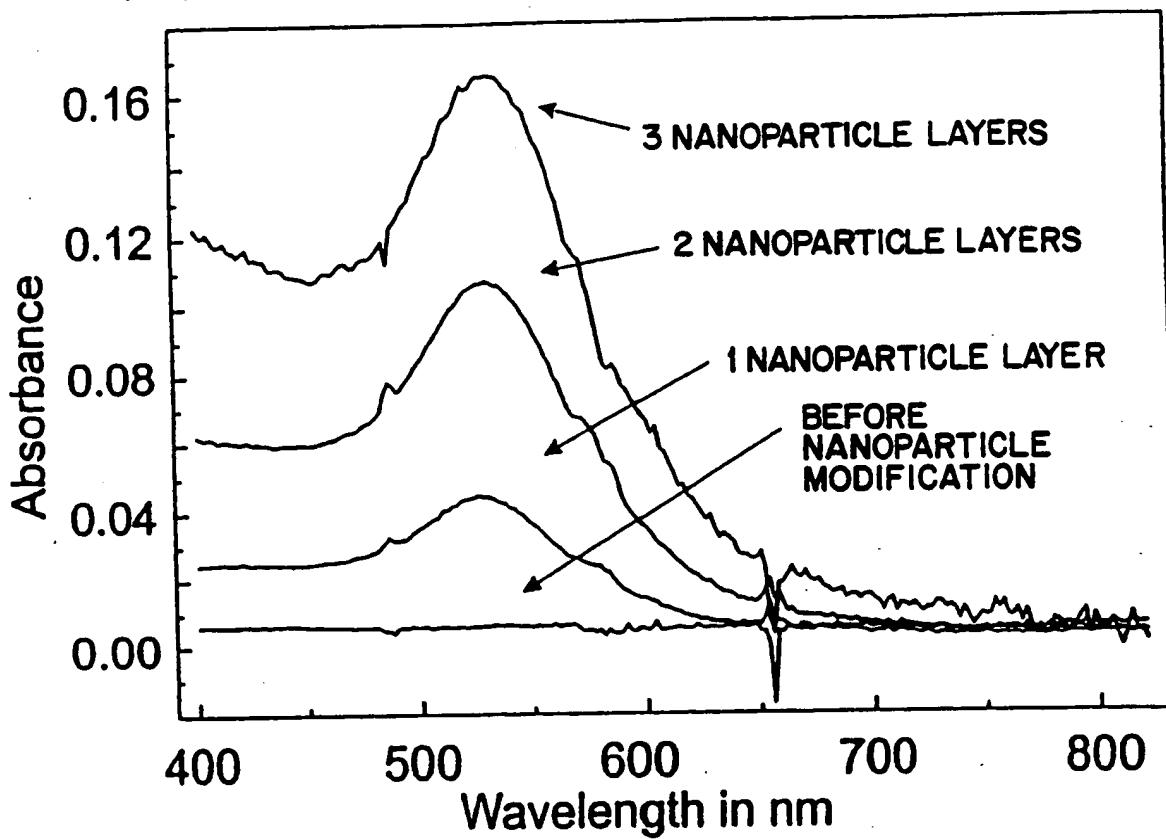
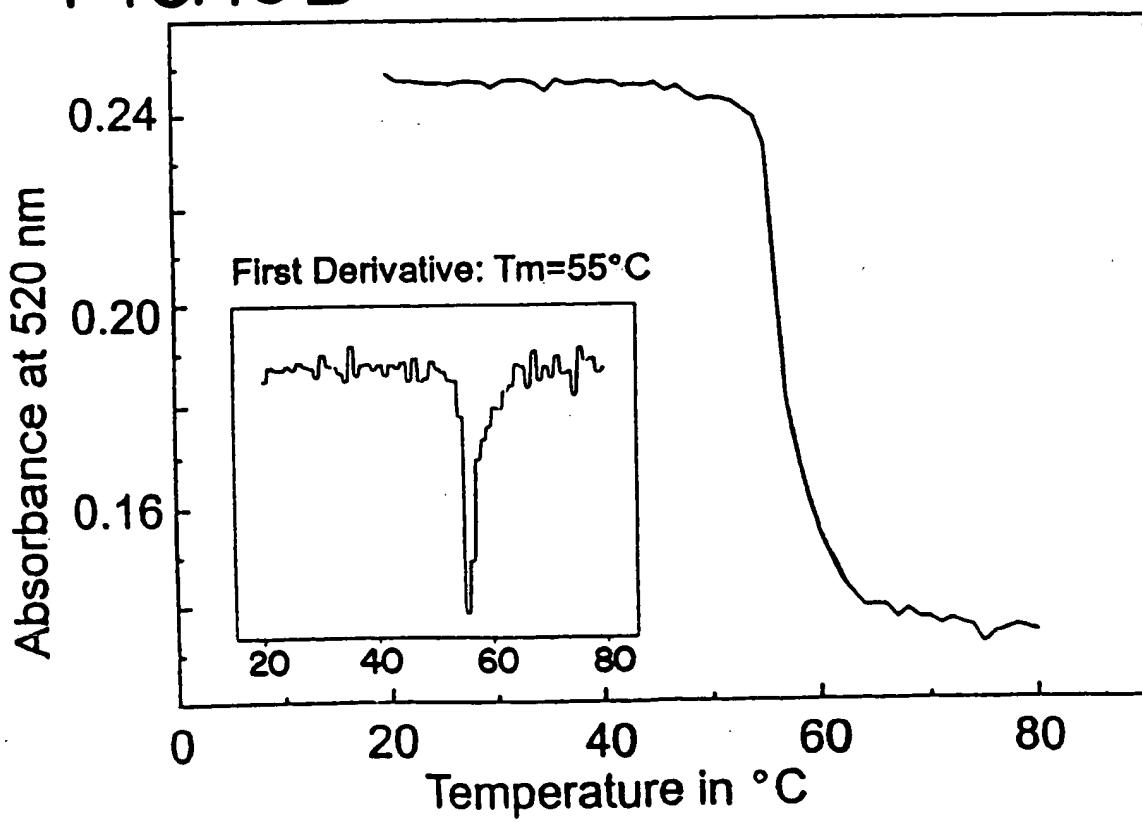


FIG. 19B



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FIG. 20A

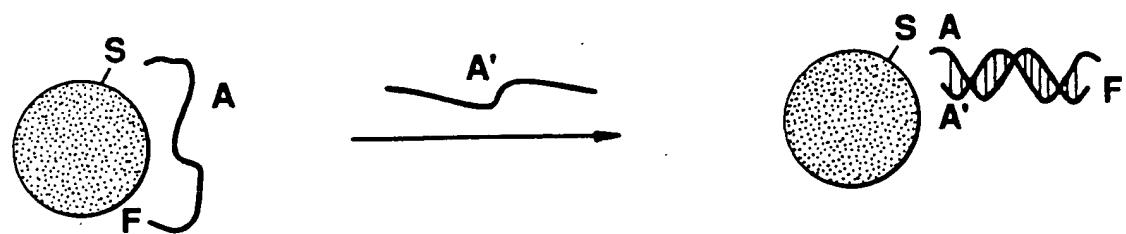
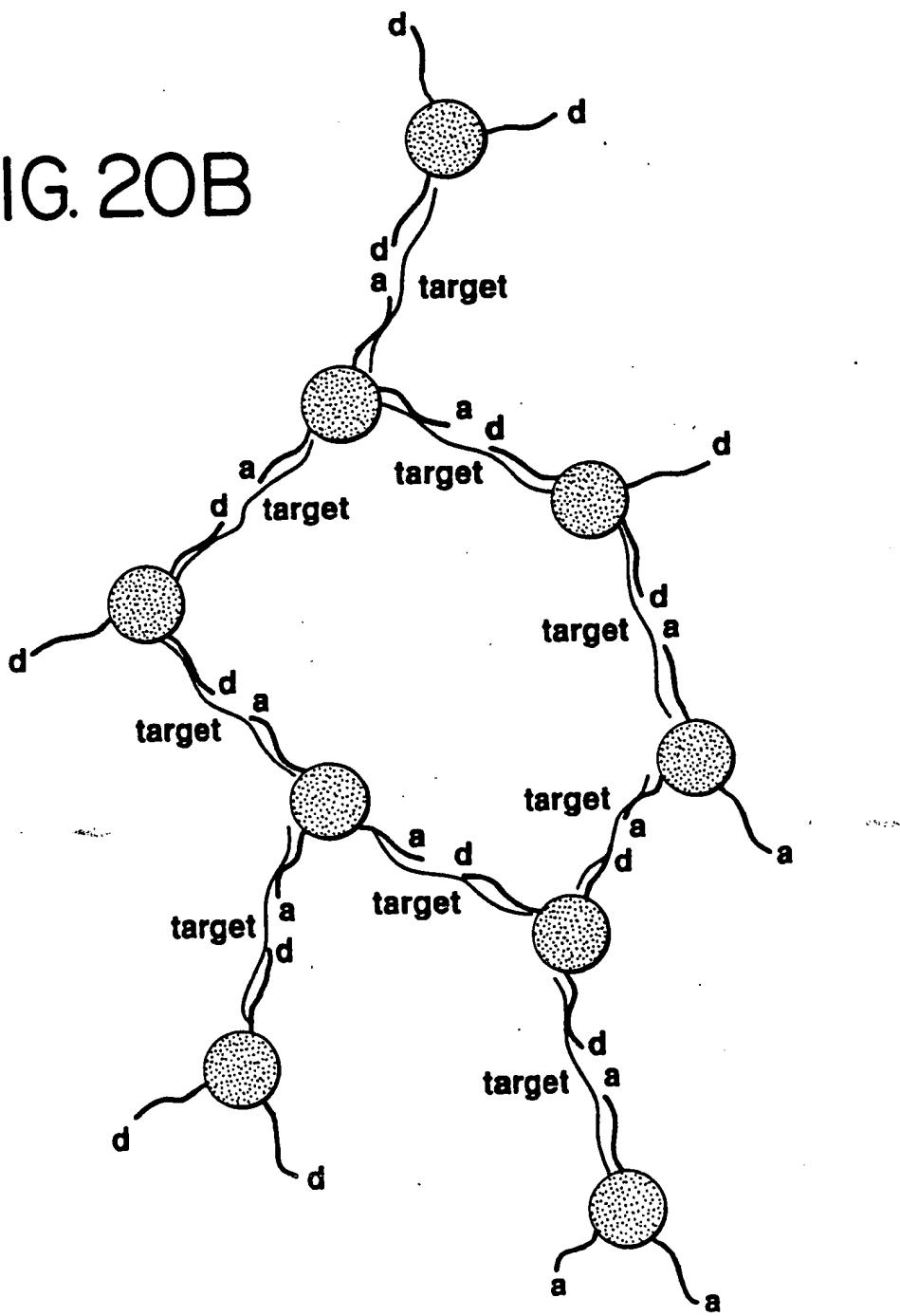


FIG. 20B



# FIG. 2

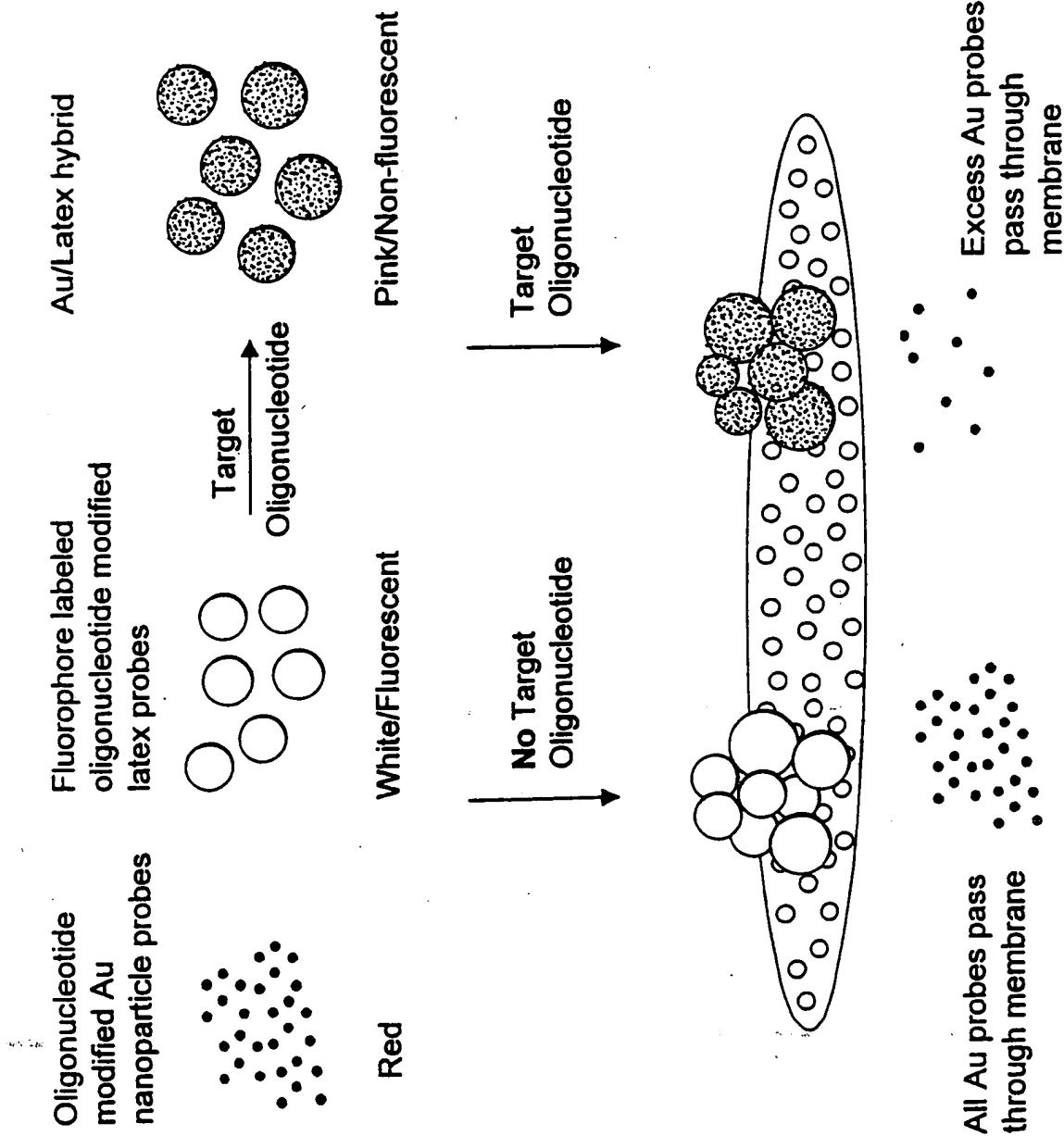
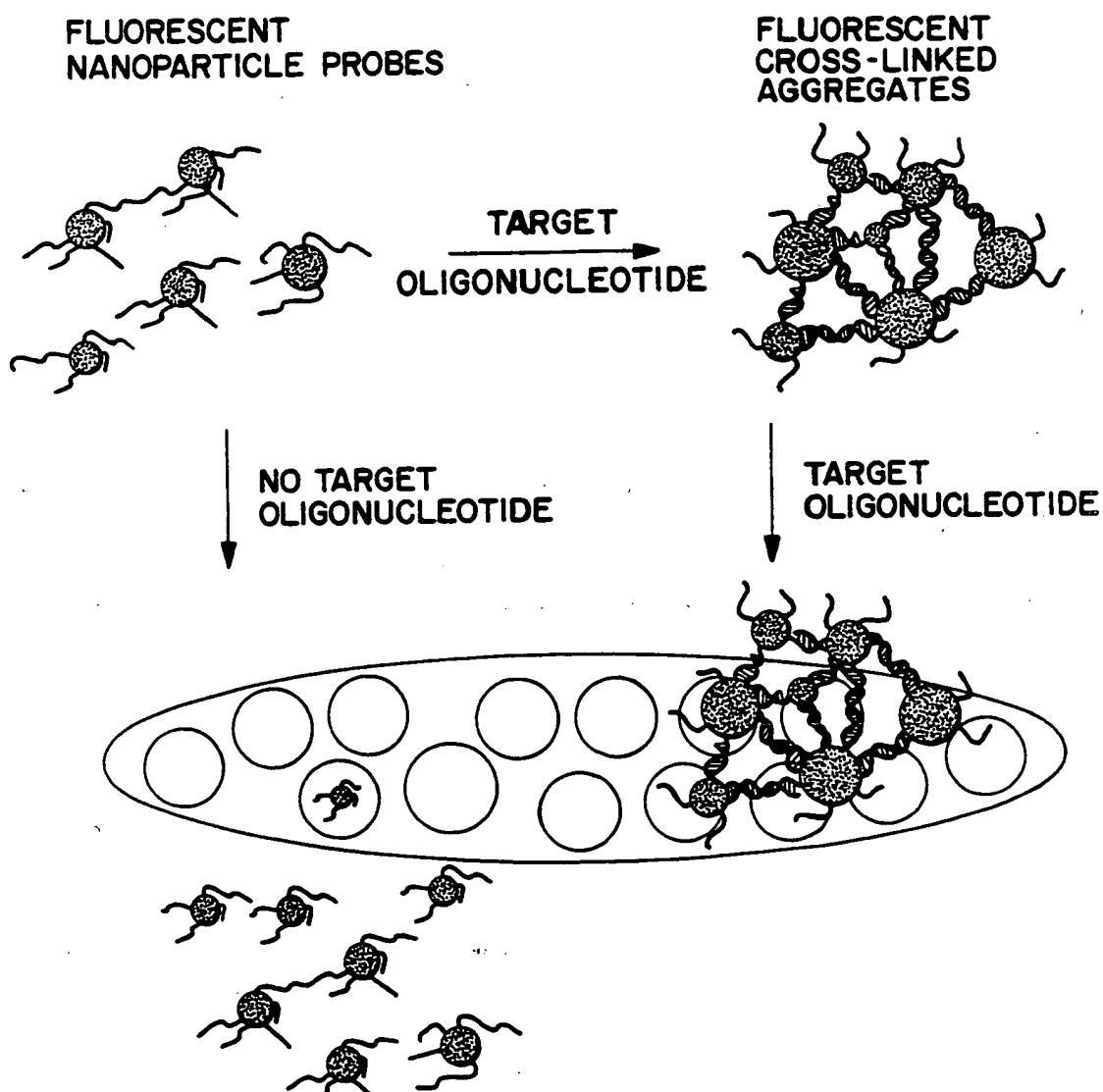


FIG. 22



THE FLUORESCENT NANOPARTICLE  
PROBES PASS THROUGH THE  
MEMBRANE

THE FLUORESCENT  
CROSS-LINKED AGGREGATES  
ARE RETAINED BY THE  
MEMBRANE

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# FIG. 23

## Anthrax PCR Product

5' G GCG GAT GAG TCA GTA GTT AAG GAG GCT CAT AGA GAA GTA ATT AAT  
3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GTA TCT CTT CAT TAA TTA

TCG TCA ACA GAG GGA TTA TTG TTA AAT ATT GAT AAG GAT ATA AGA AAA  
AGC AGT TGT CTC CCT AAT AAC AAT TTA TAA CTA TTC CTA TAT TCT TTT

ATA TTA TCC AGG GTT ATA TTG TAG AAA TTG AAG ATA CTG AAG GGC TT 3'  
TAT AAT AGG TCC CAA TAT AAC ATC TTT AAC TTC TAT GAC TTC CCG AA 5'

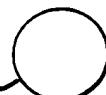
**141 mer Anthrax PCR product [SEQ ID NO:36]**

3' CTC CCT AAT AAC AAT



[SEQ ID NO:37]

3' TTA TAA CTA TTC CTA



[SEQ ID NO:38]

Oligonucleotide-Nanoparticle Probes

## Blocker Oligonucleotides

3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GT  
3' A TCT CTT CAT TAA TTA AGC AGT TGT  
3' TAT TCT TTT TAT AAT AGG TCC CAA TAT  
3' AAC ATC TTT AAC TTC TAT GAC TTC CCG AA

[SEQ ID NO:39]

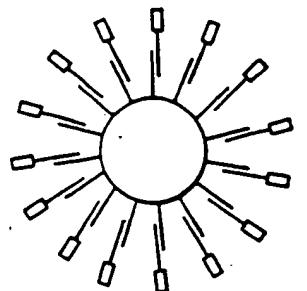
[SEQ ID NO:40]

[SEQ ID NO:41]

[SEQ ID NO:42]

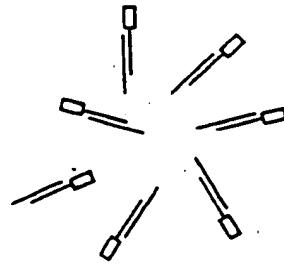
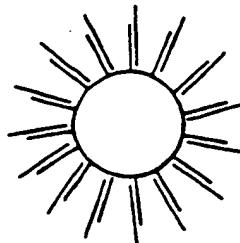
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FIG. 24

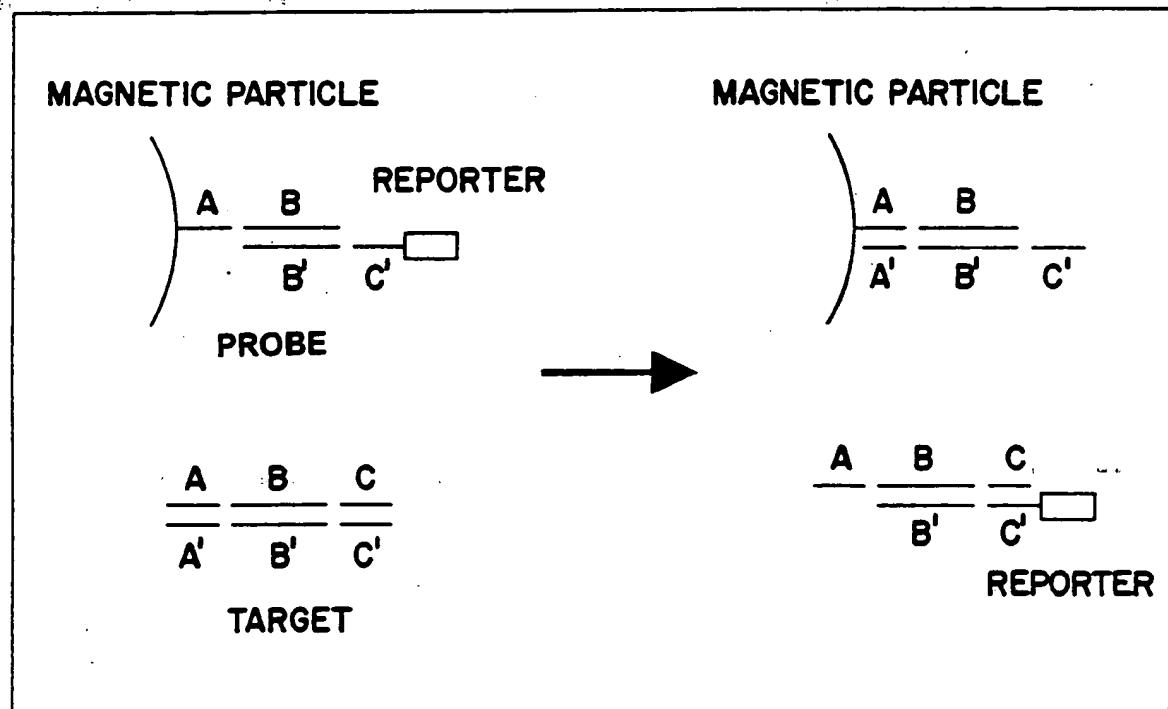


SATELLITE PROBE

TARGET  
→



DETECTION SIGNAL



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FIG. 25A

1. (TARGET)

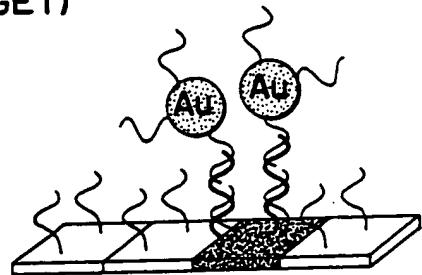
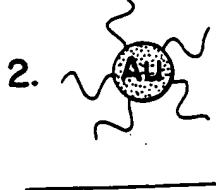
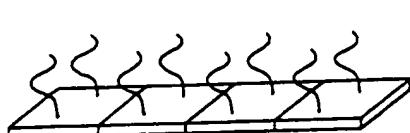


FIG. 25B

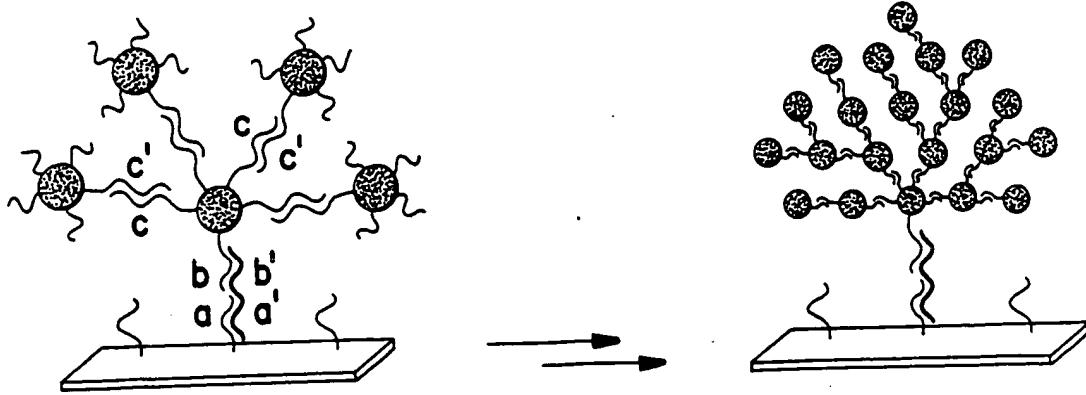
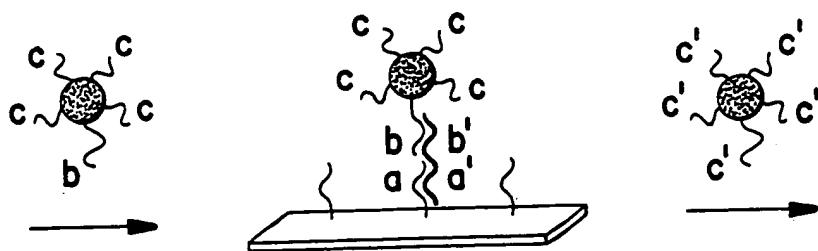
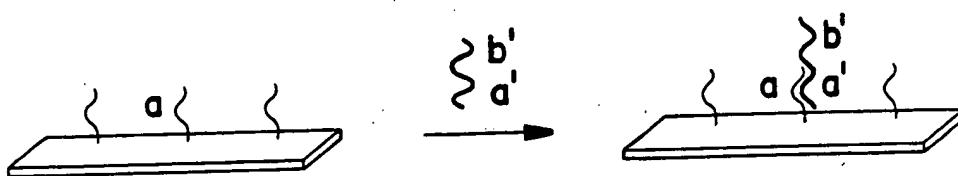


FIG. 26A

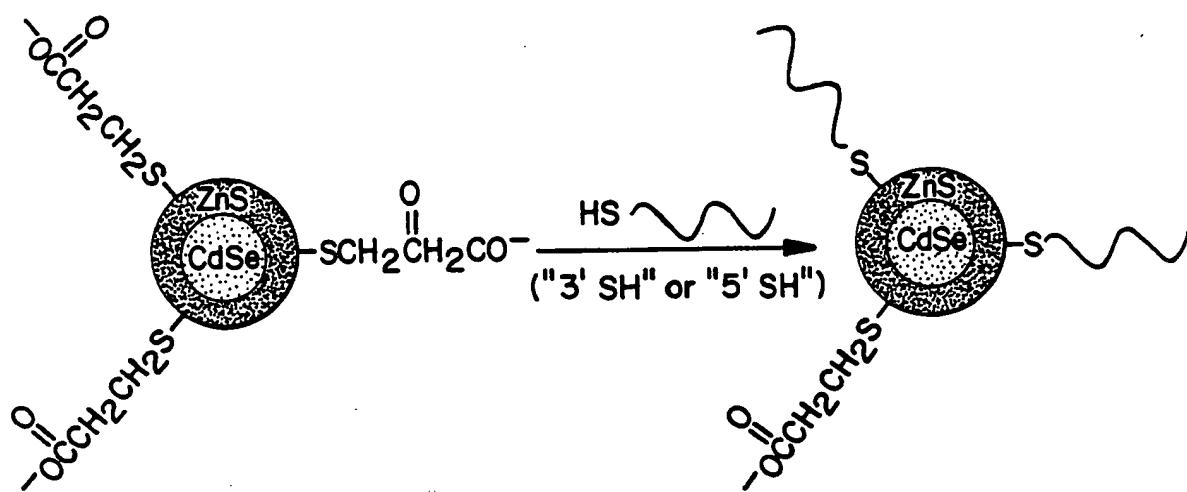


FIG. 26B

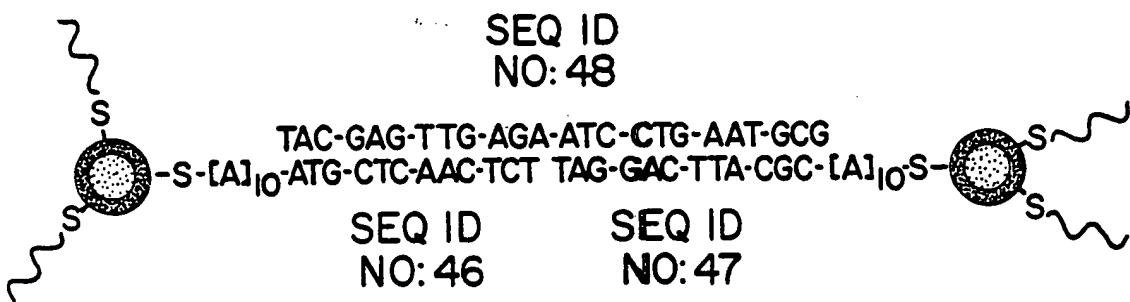


FIG. 27A

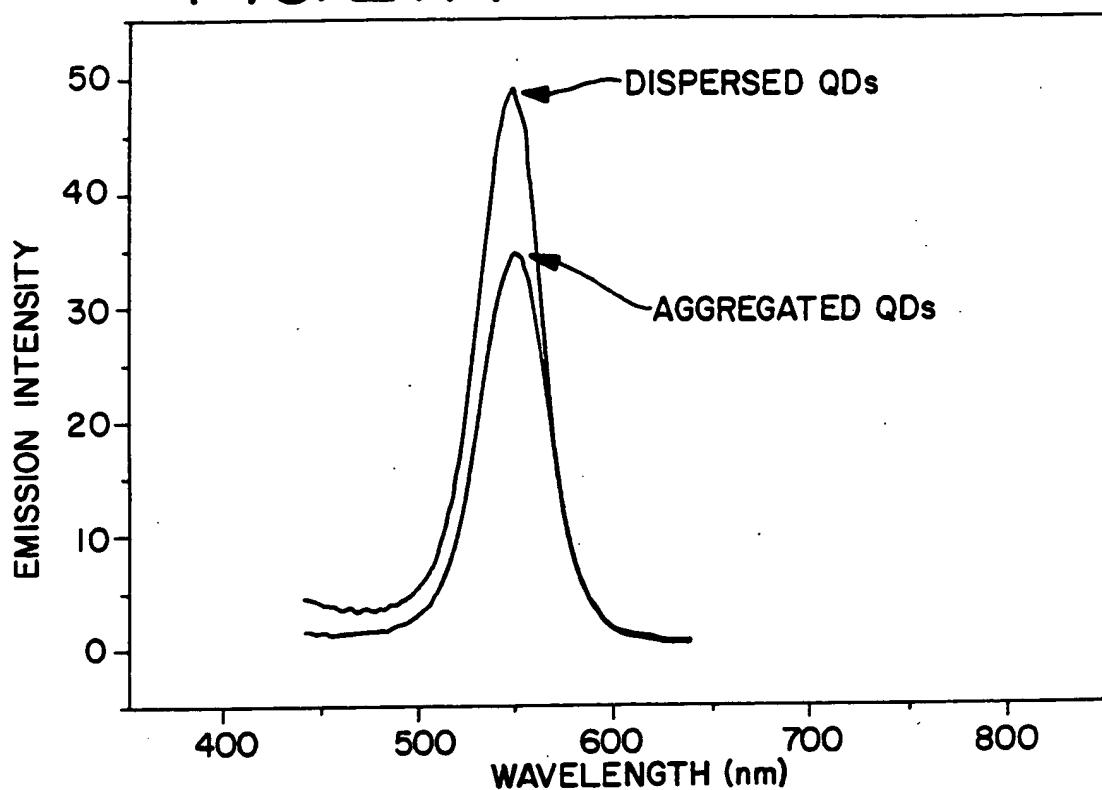
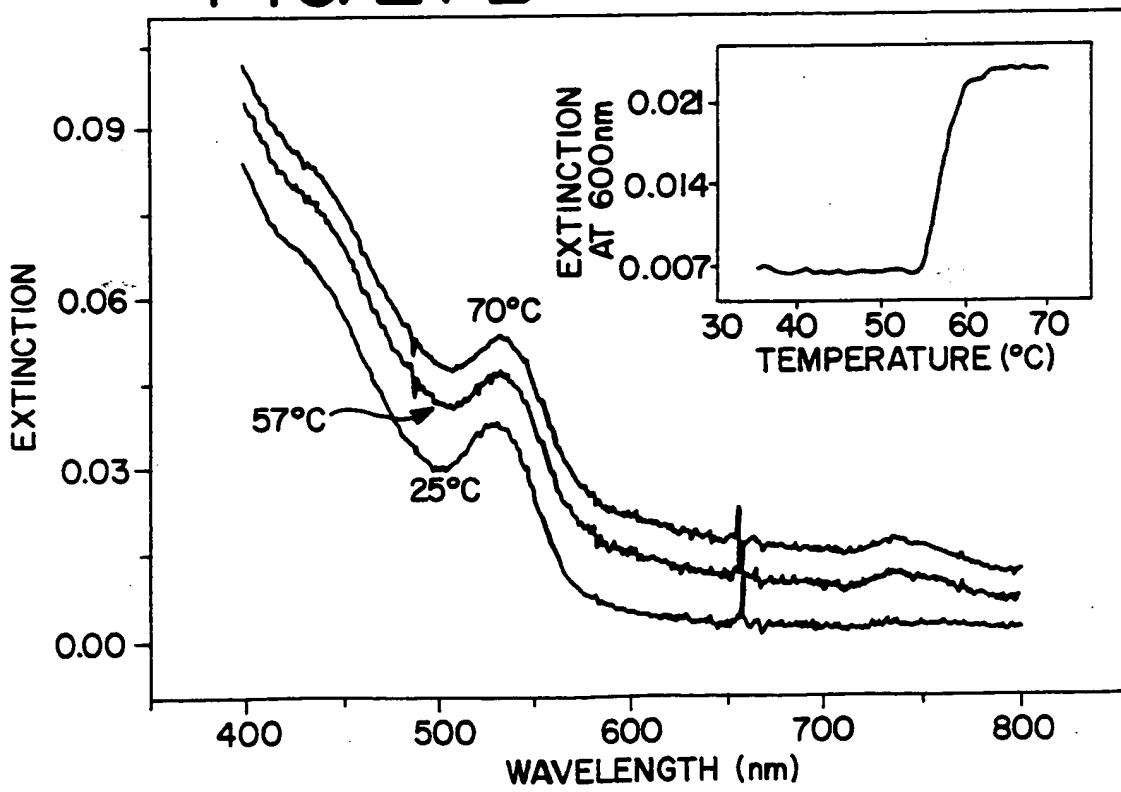


FIG. 27B



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FIG. 27C

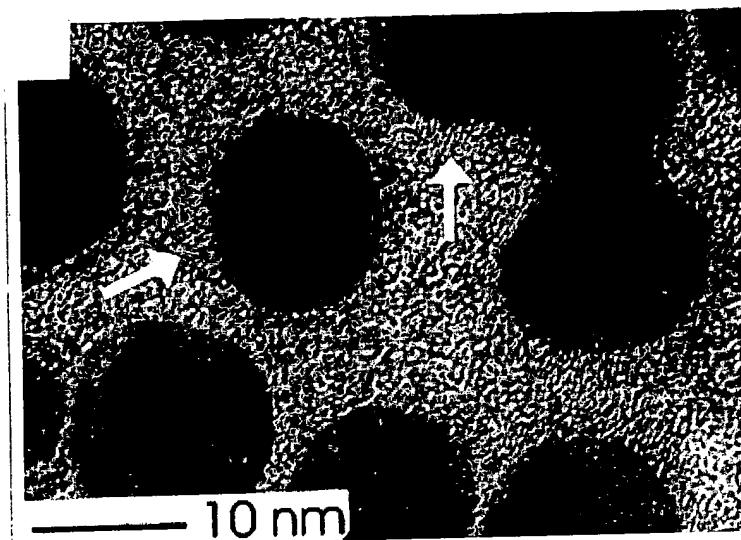


FIG. 27D

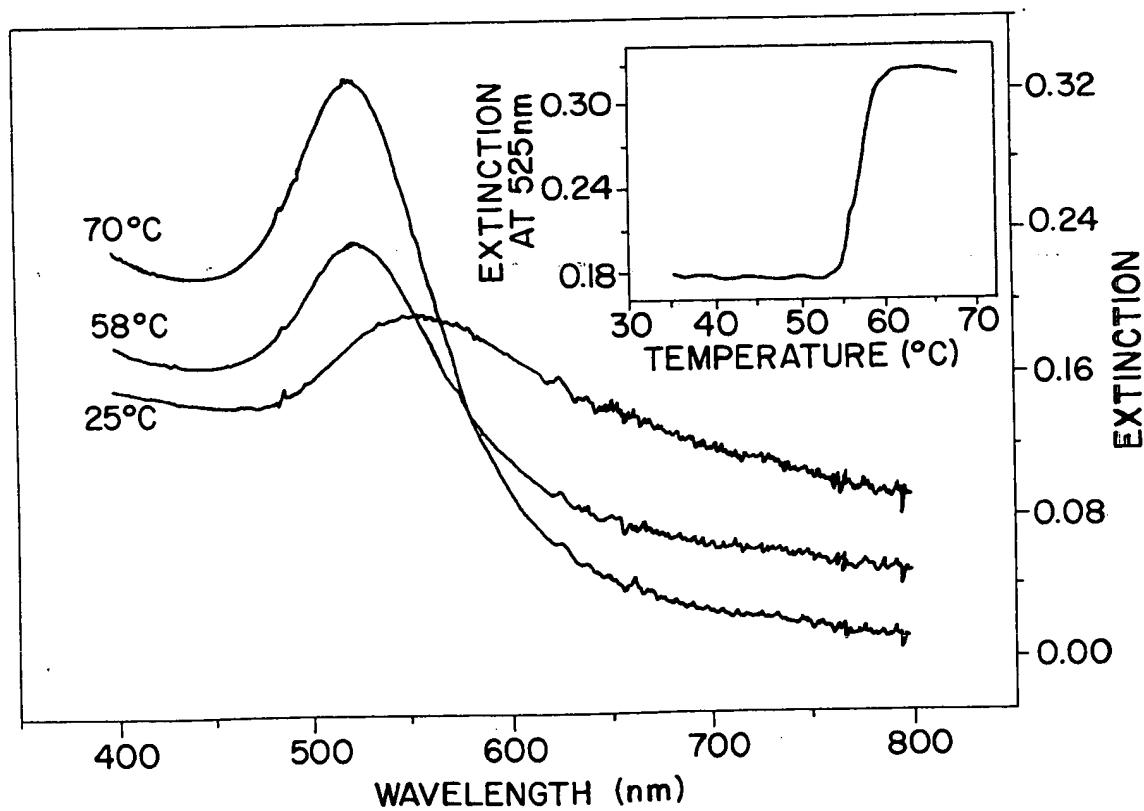


FIG. 28A

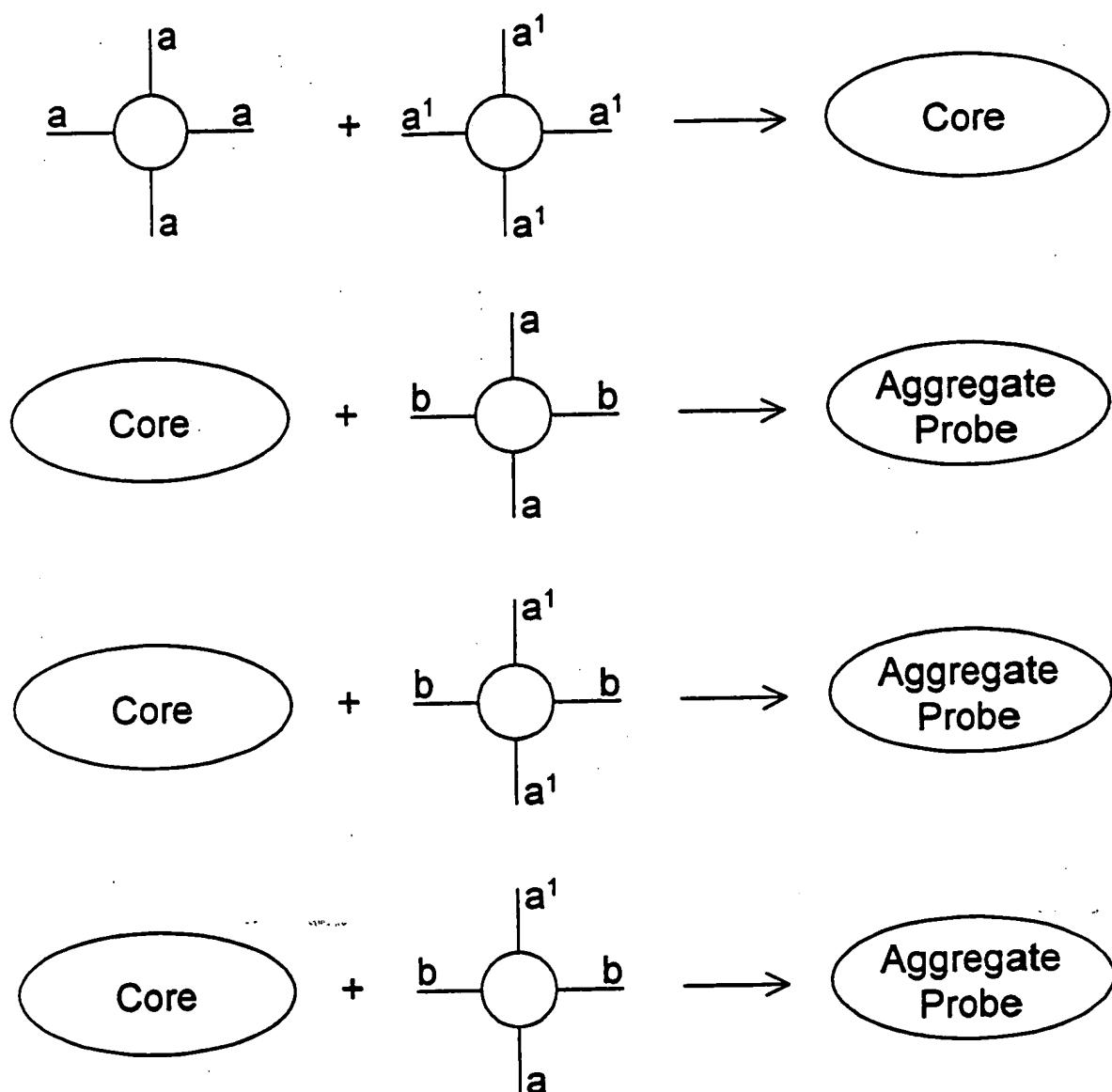


FIG. 28B

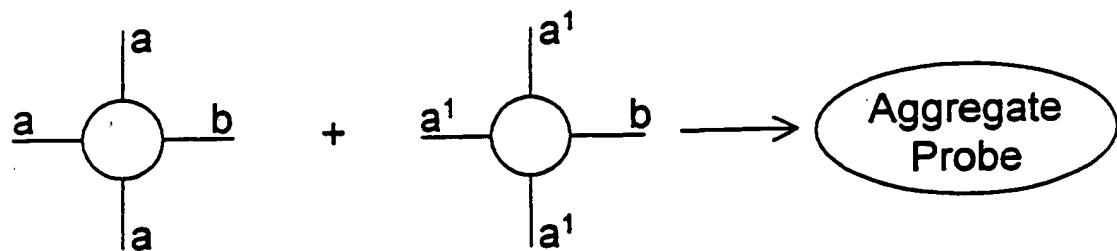


FIG. 28C

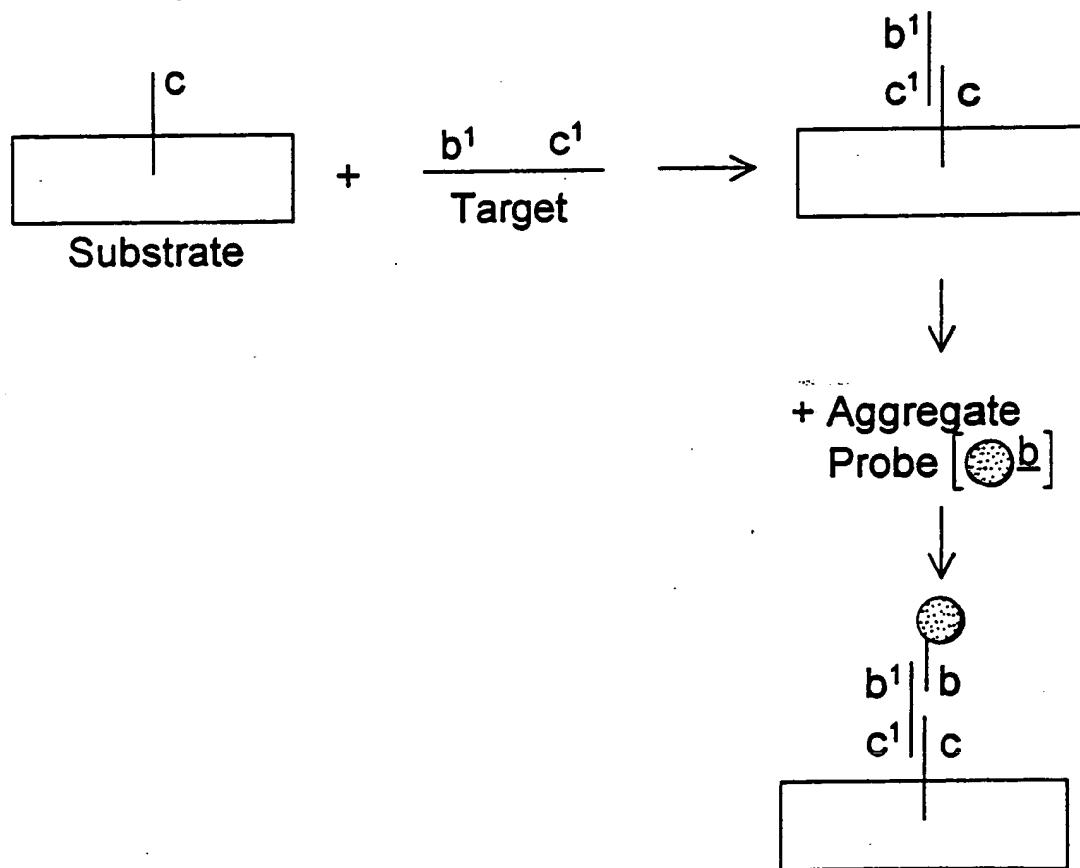


FIG. 28D

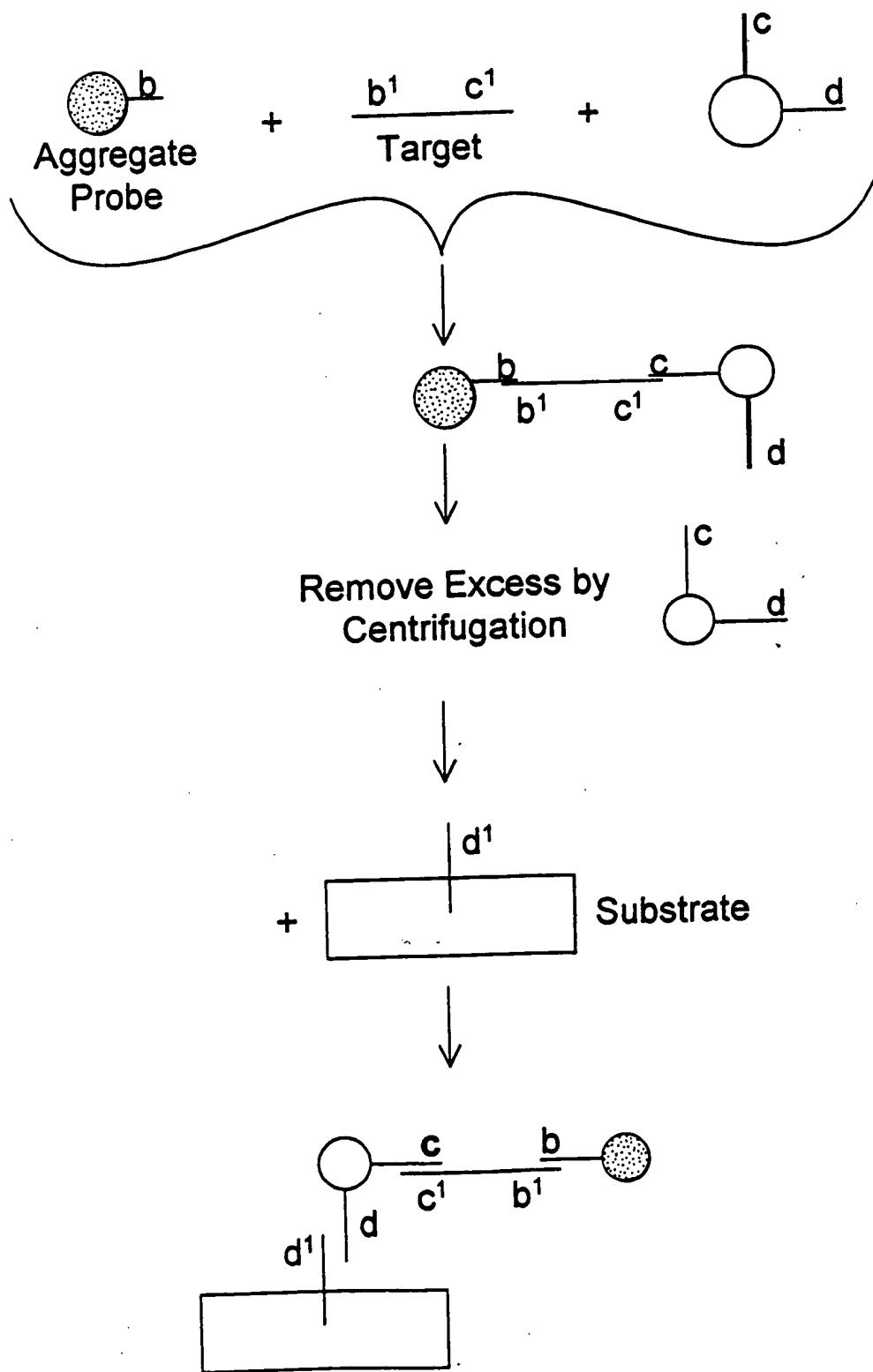


FIG. 28E

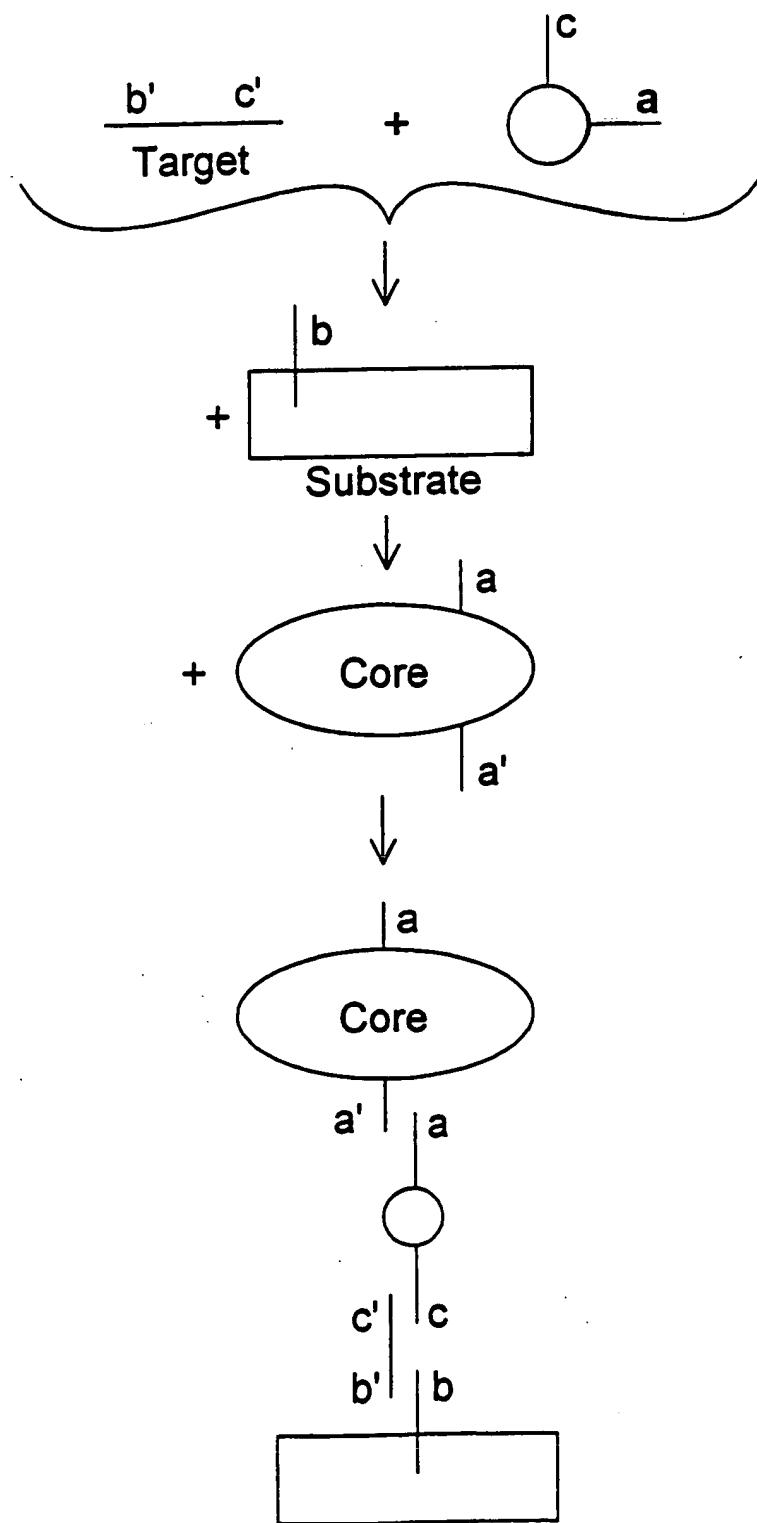


FIG. 29

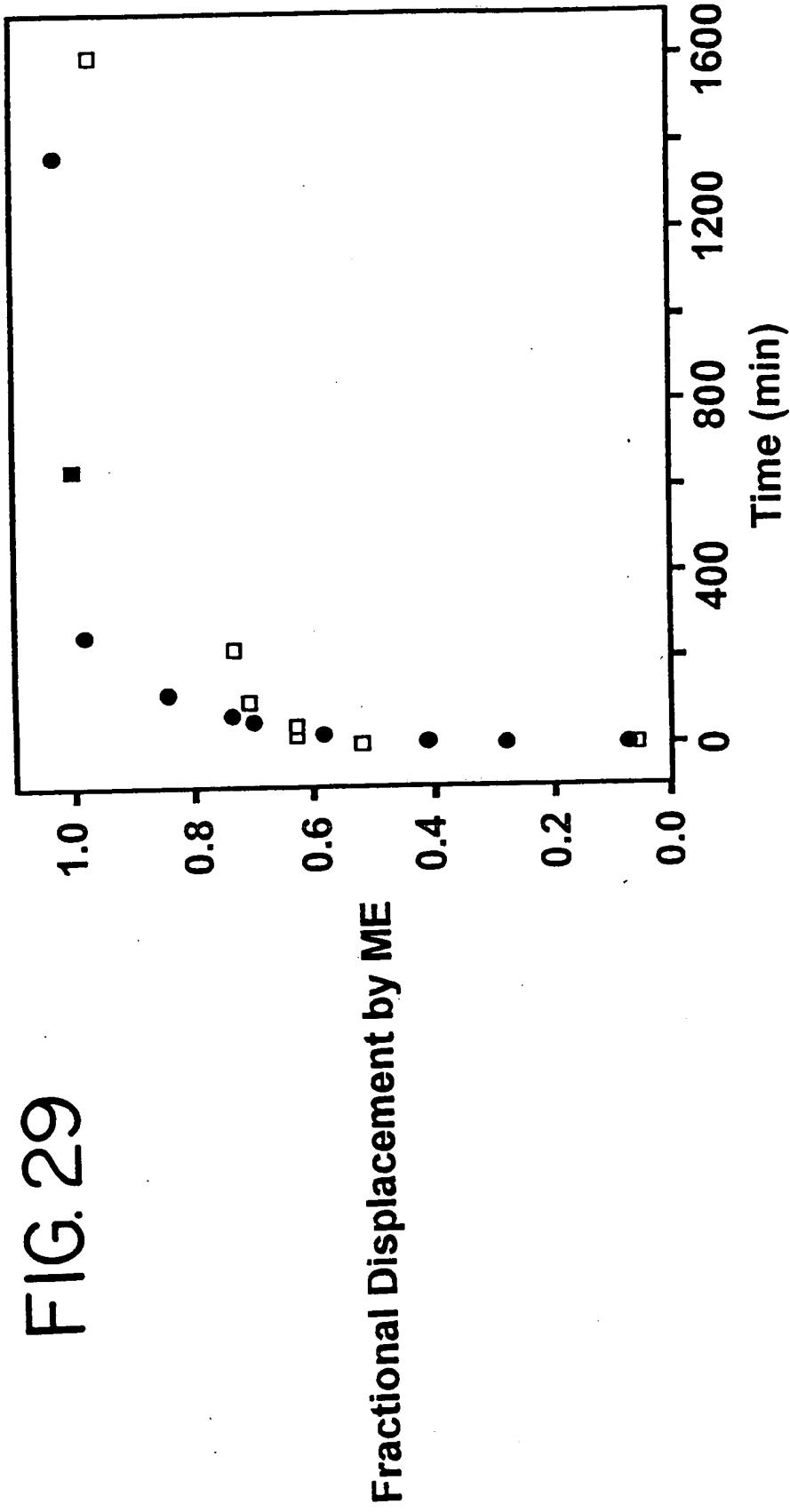


FIG. 30

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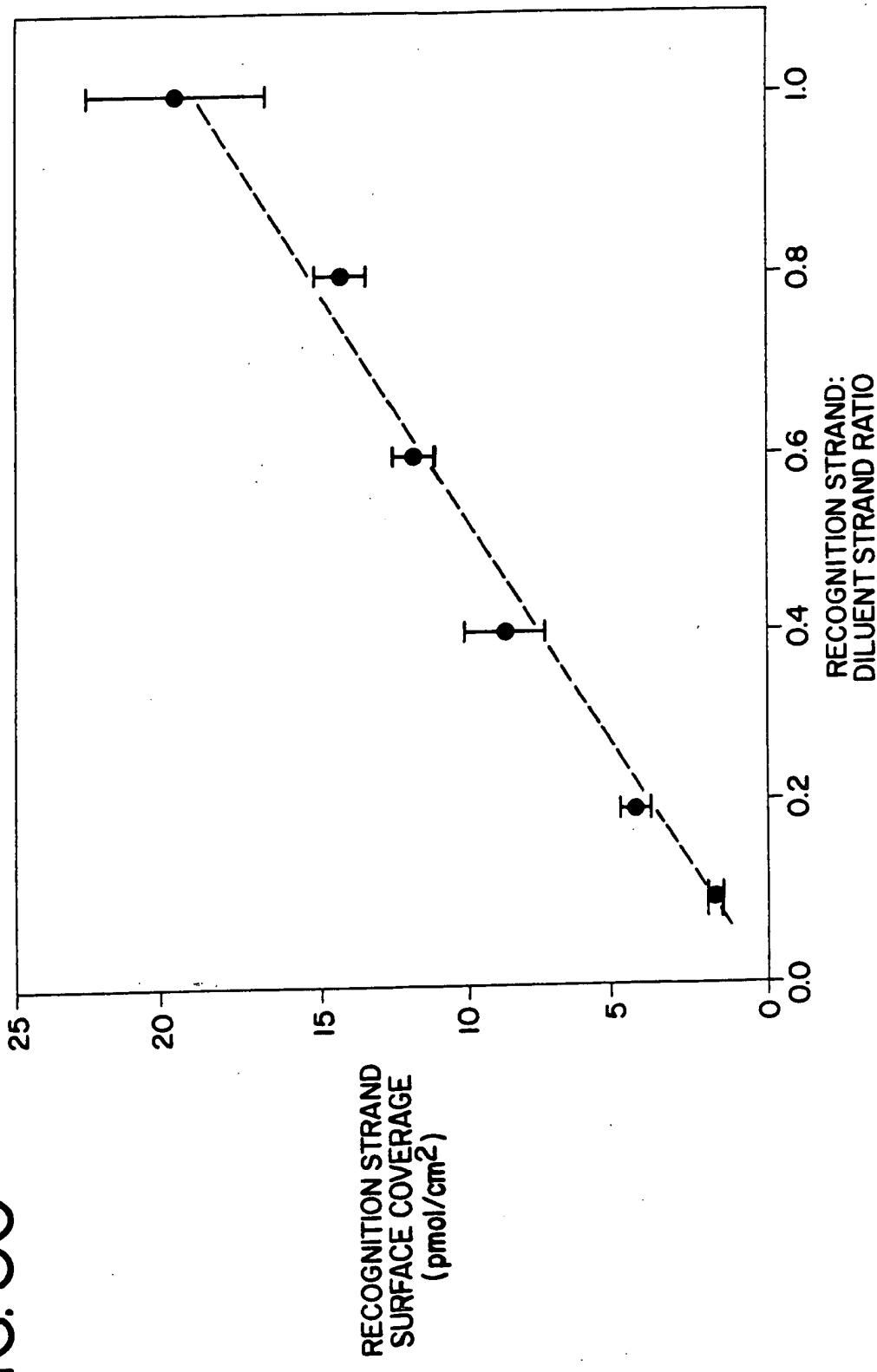
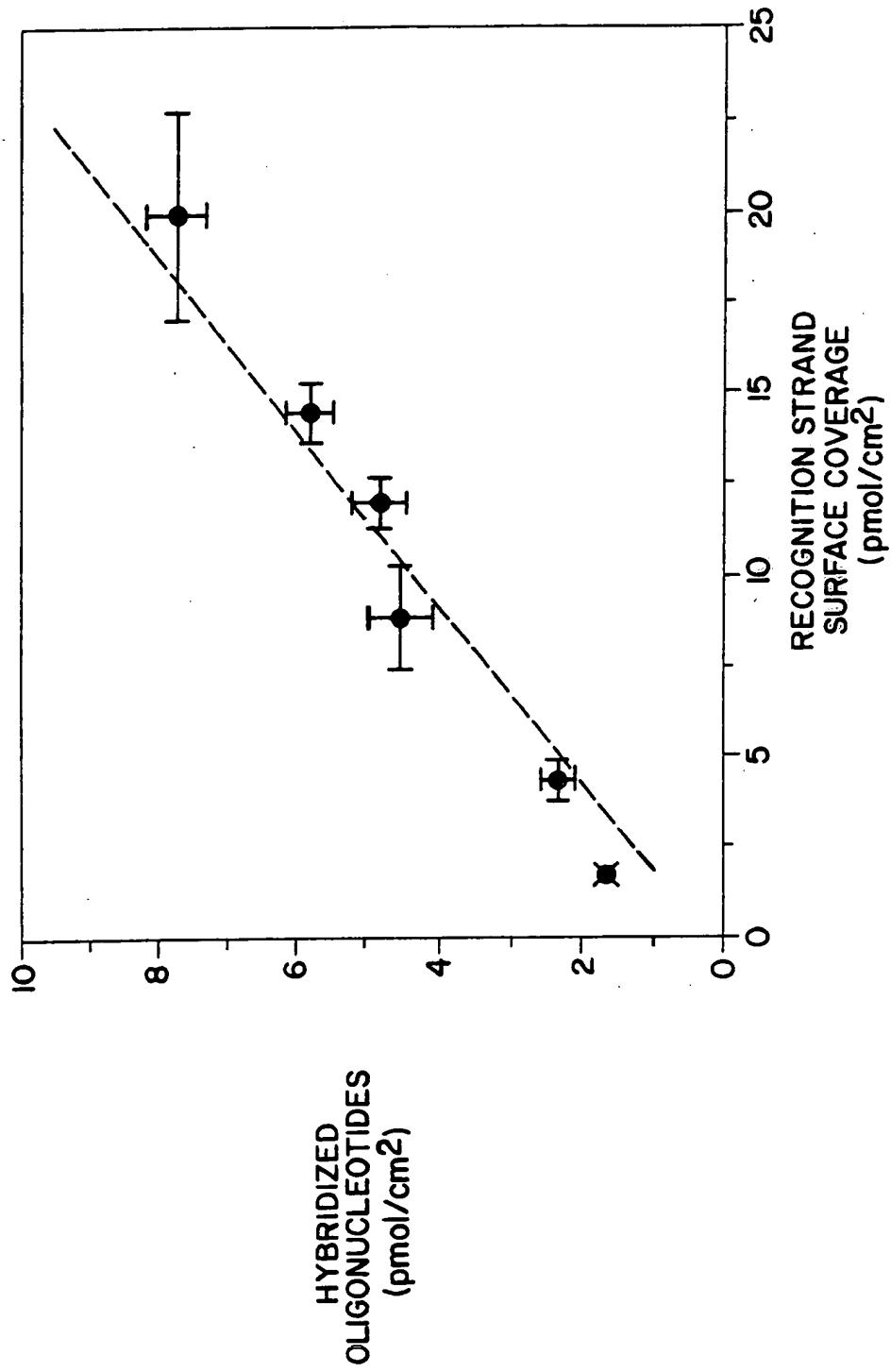


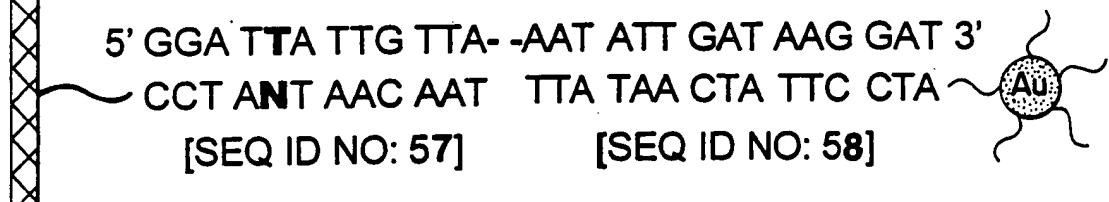
FIG. 3I

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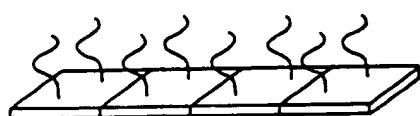
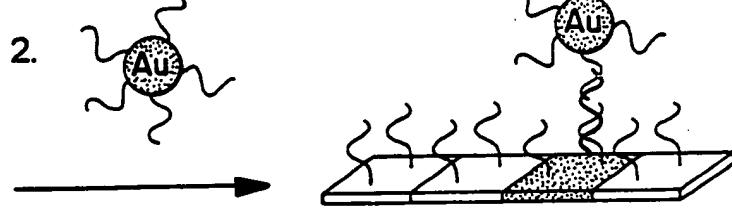
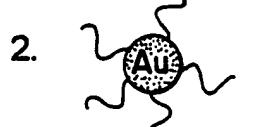
## FIG. 32

[SEQIDNO:56]

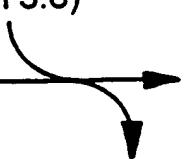


**N** = A (complementary),  
 G,C,T (mismatched)

1. ~~~ (target DNA)



$\text{Ag}^+$   
 hydroquinone  
 (pH 3.8)



$\text{Ag}(s)$   
 quinone

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# FIG. 33

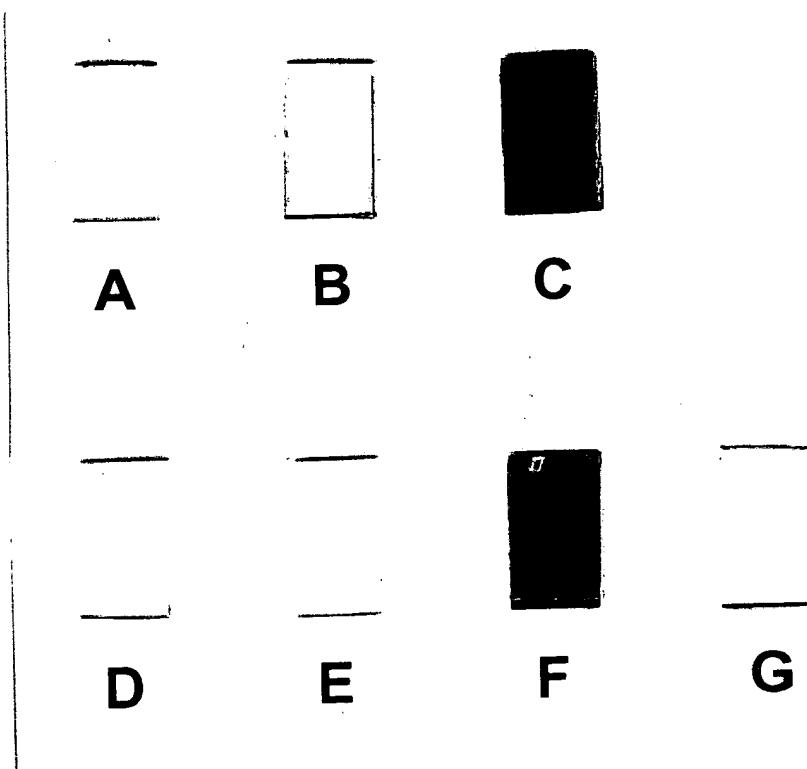
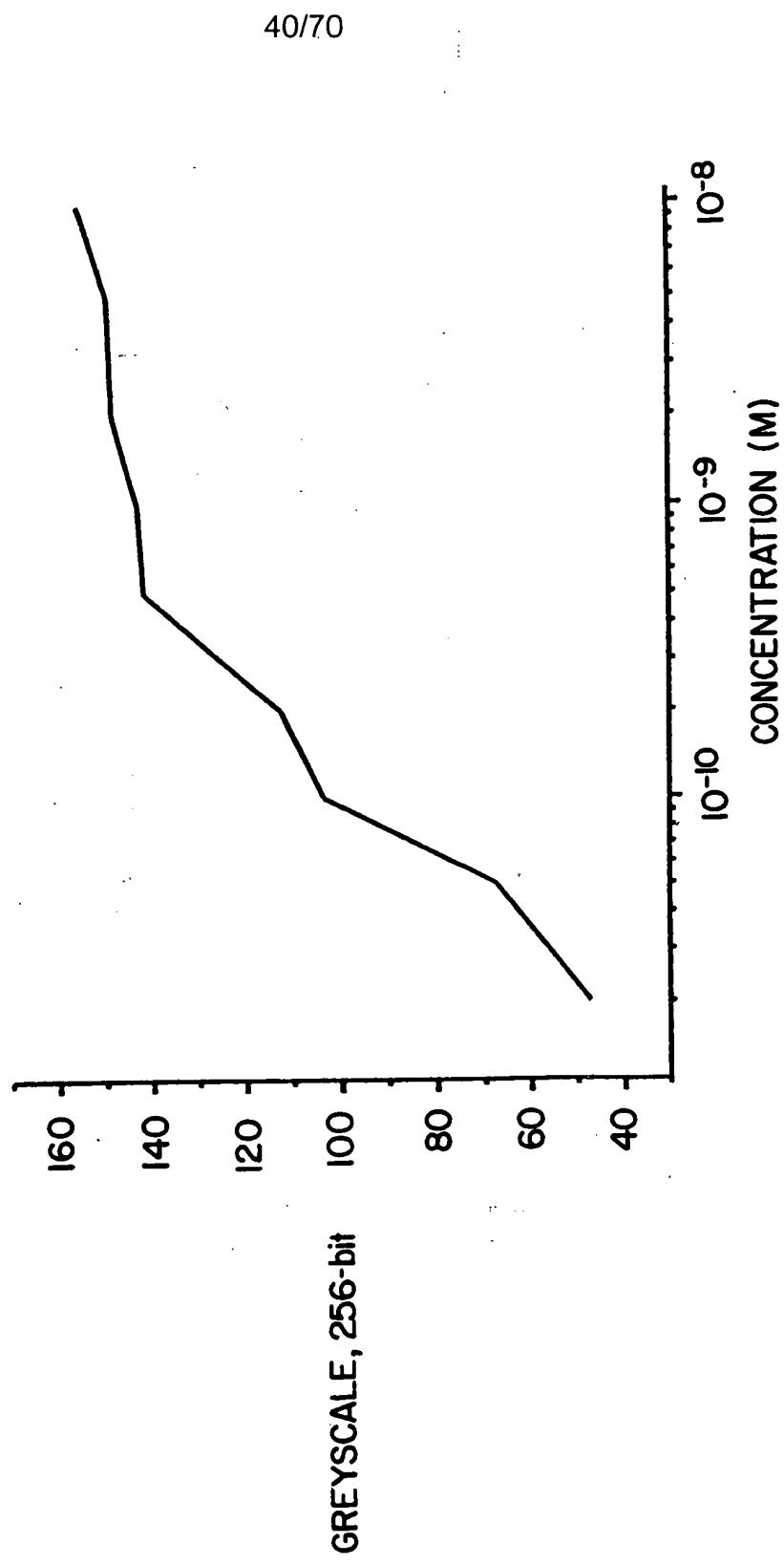


FIG. 34



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FIG.35A

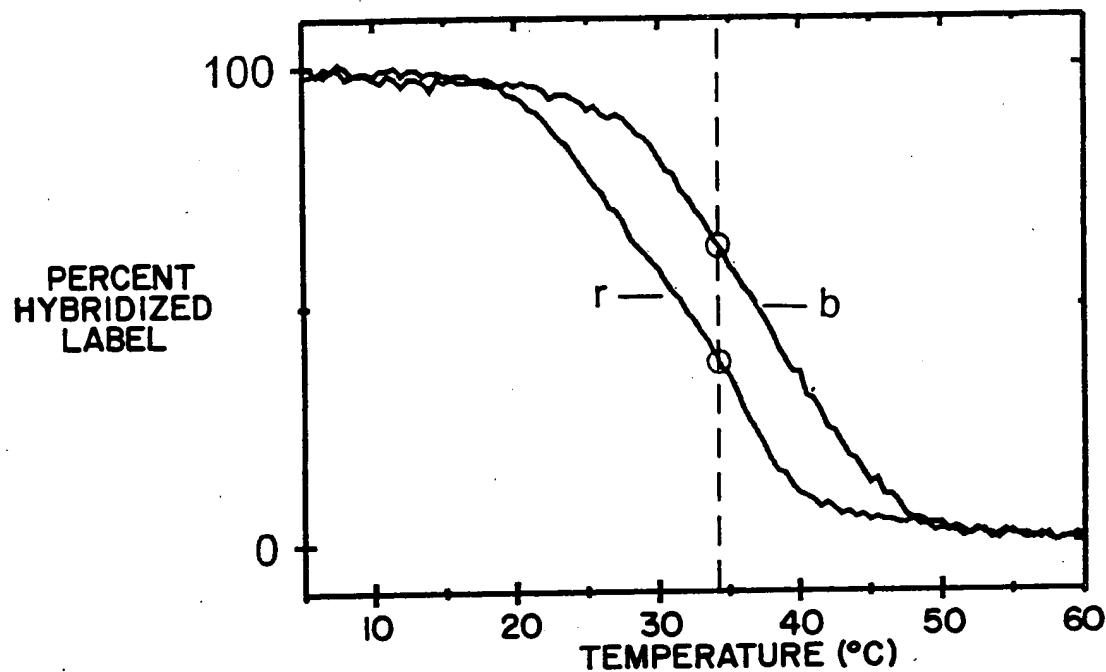
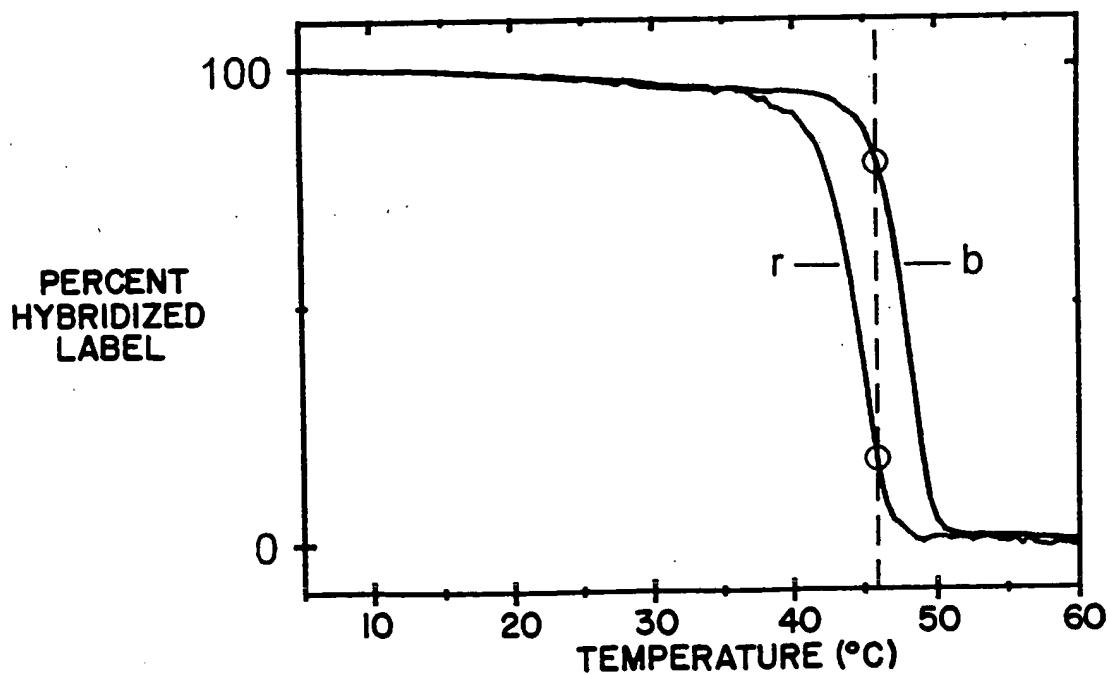
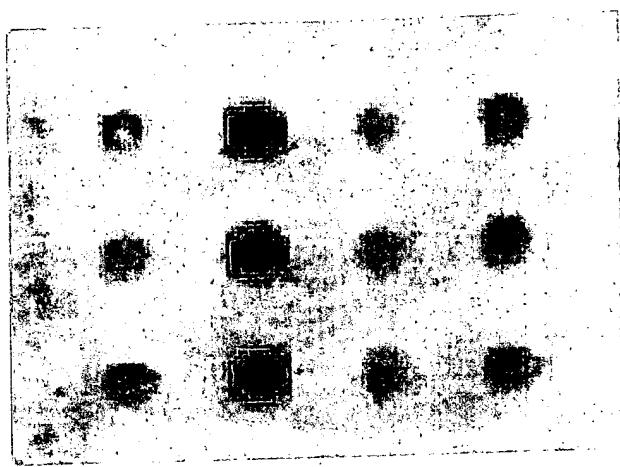


FIG.35B

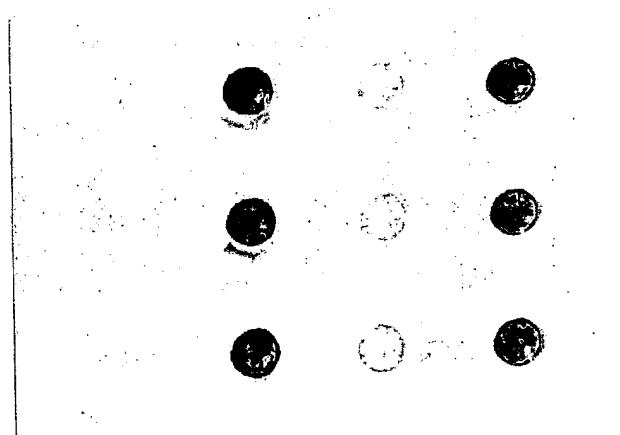


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**FIG. 36A**



**FIG. 36B**



C A T G

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FIG.37A

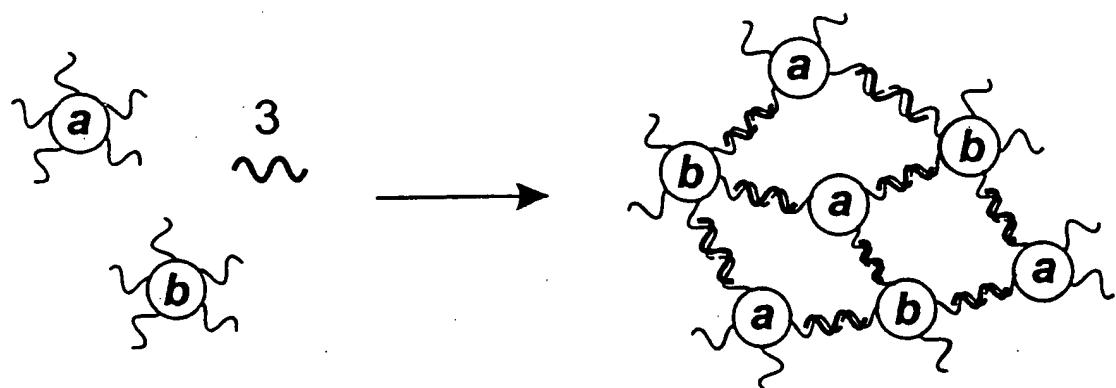
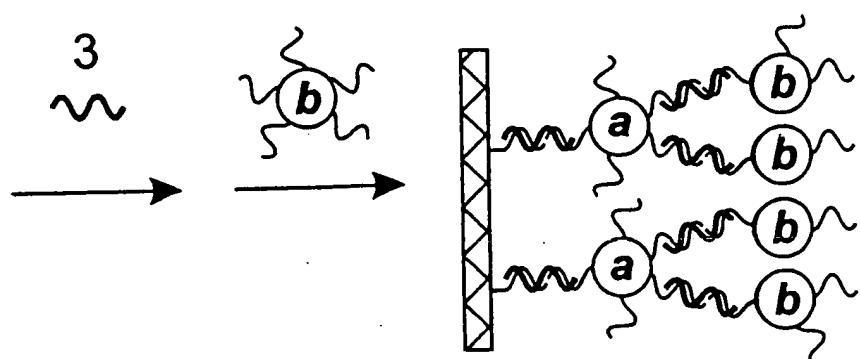
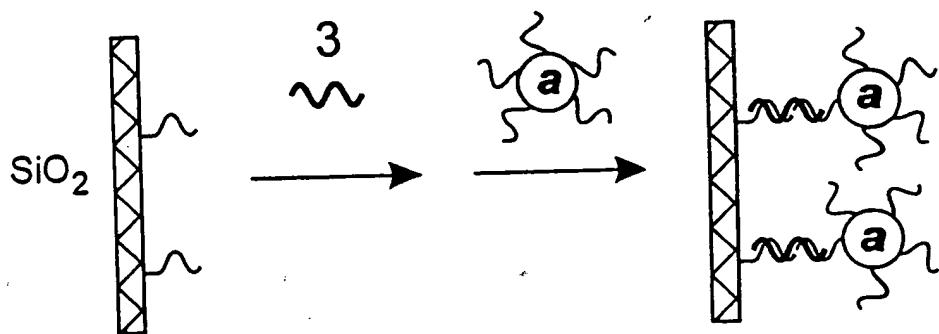
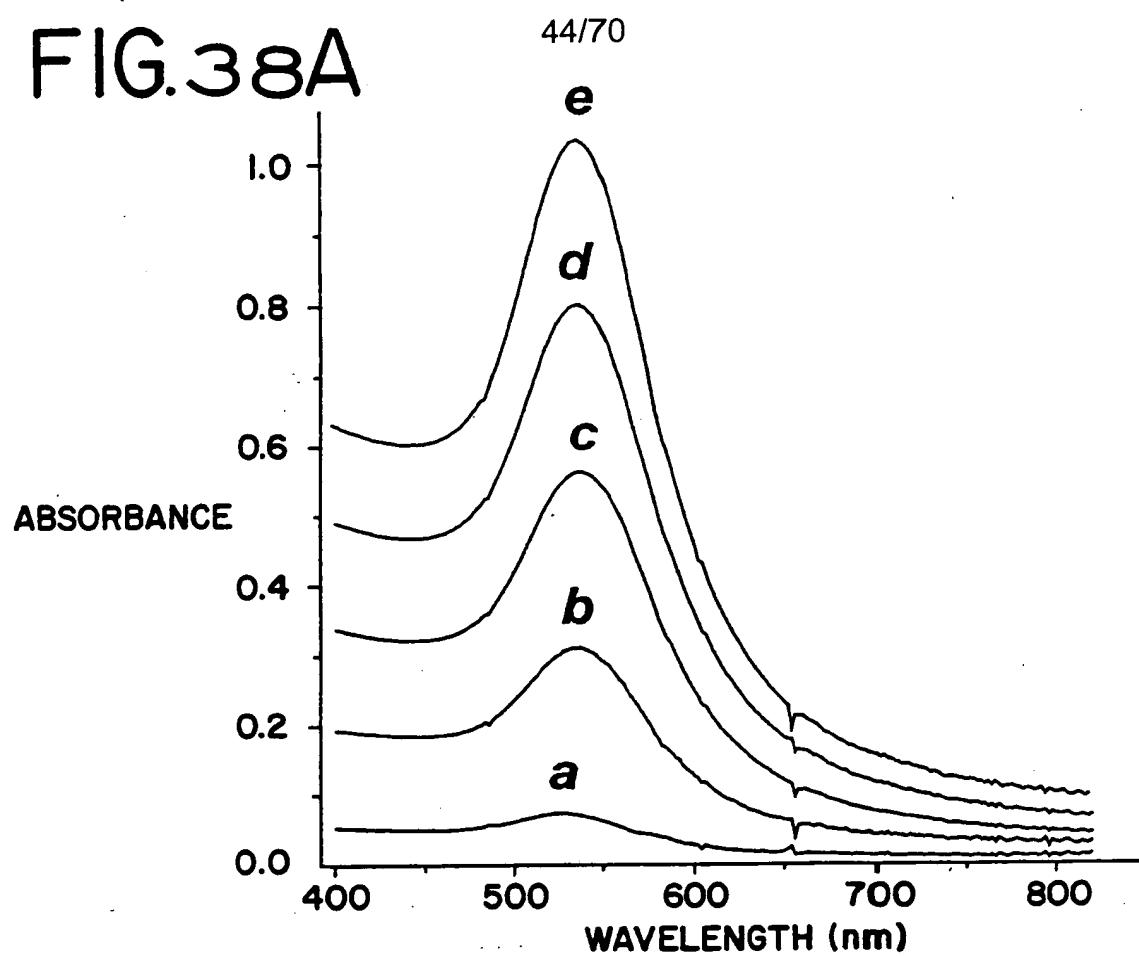


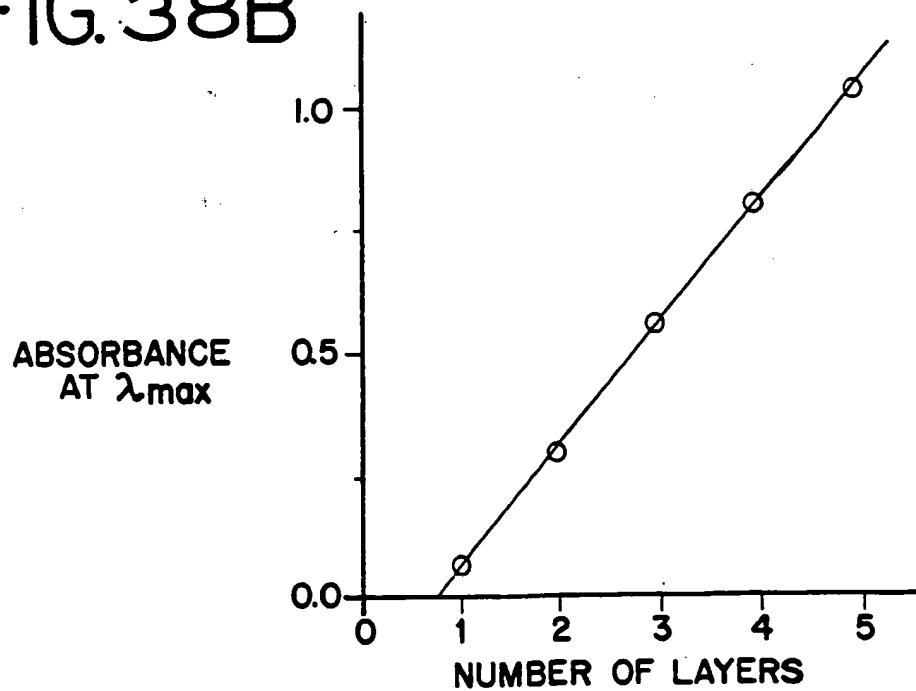
FIG.37B



**FIG.38A**

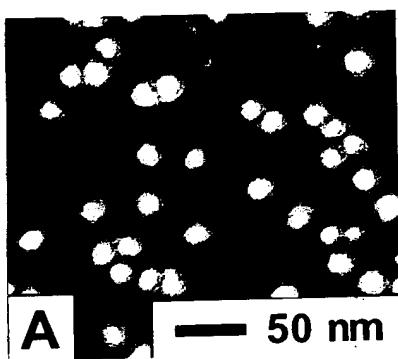


**FIG.38B**



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**FIG. 39A**



**FIG. 39B**

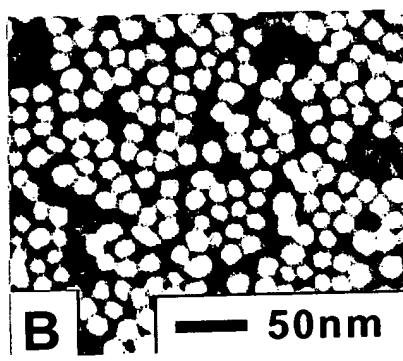


FIG.39C

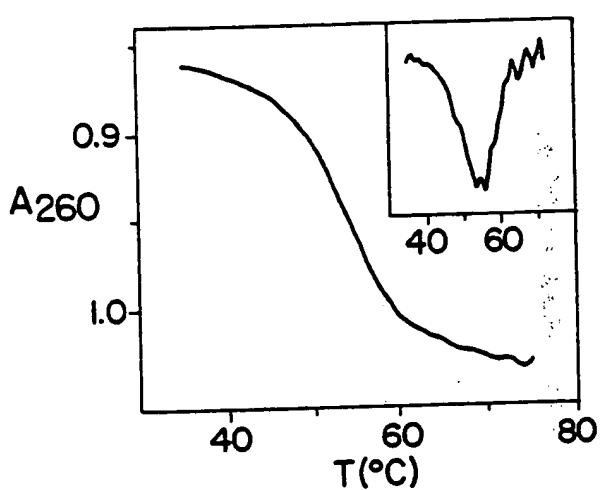


FIG.39D

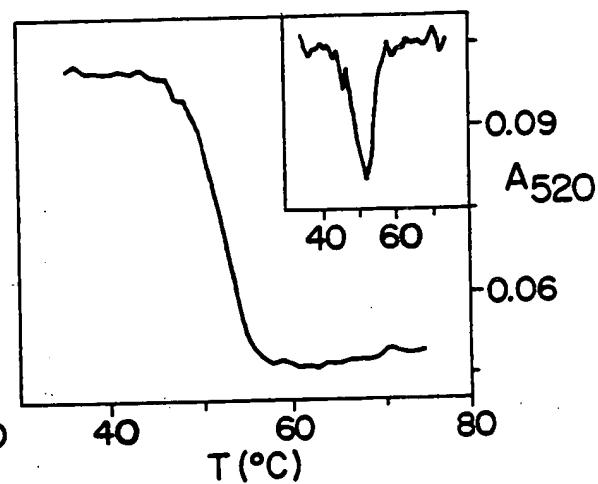


FIG.39E

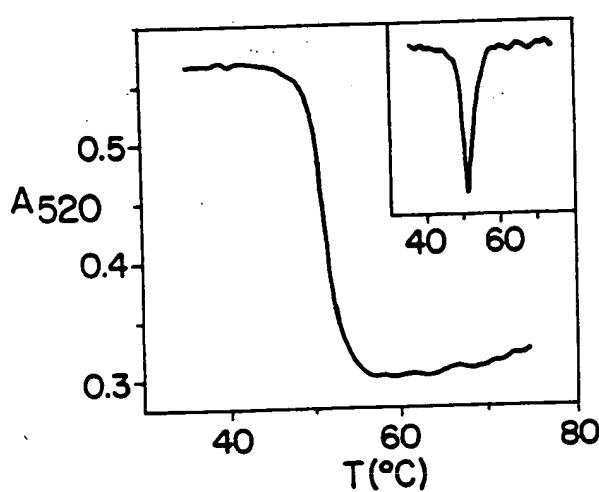
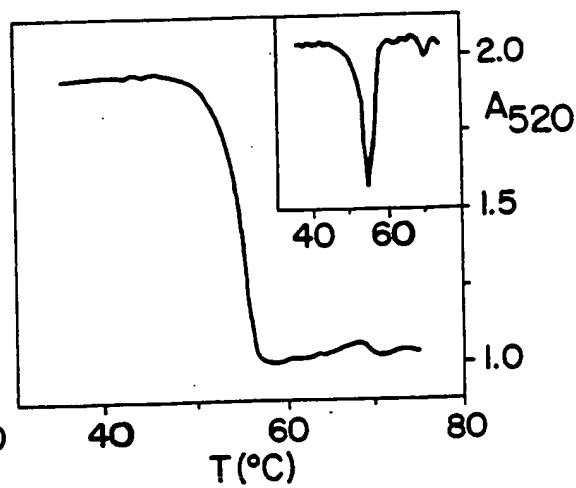


FIG.39F



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FIG. 40

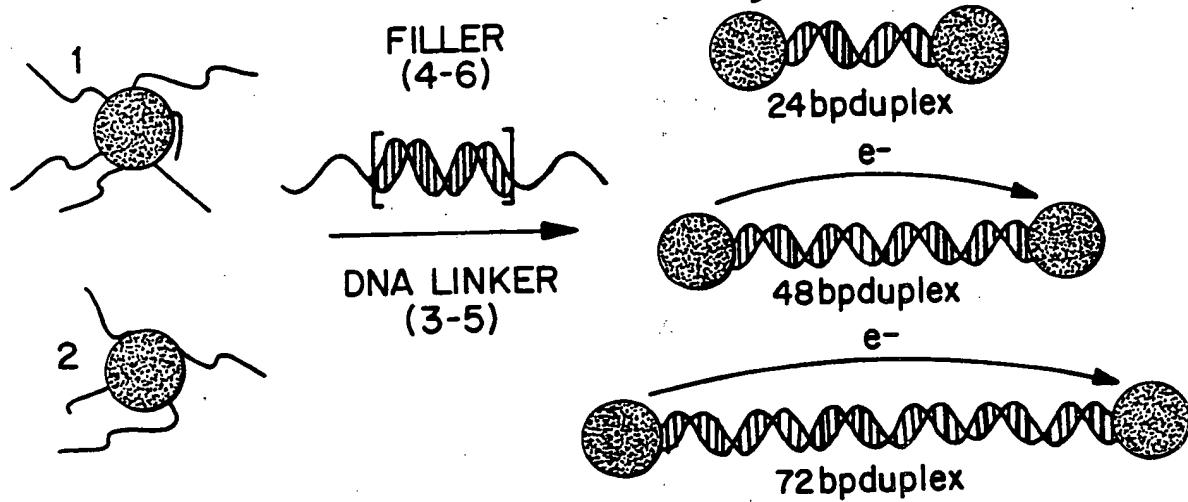
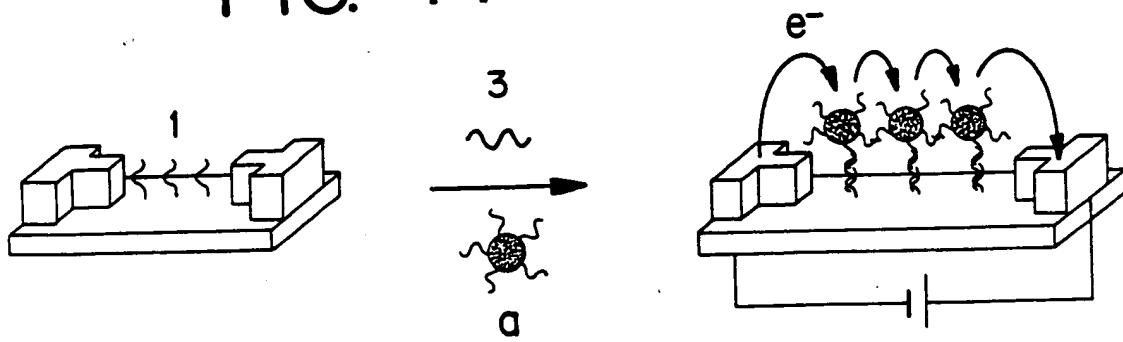
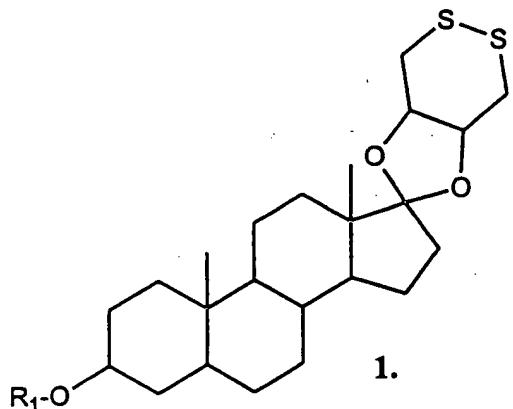


FIG. 41



## FIG. 42



**II**  $\text{HS-(CH}_2\text{)}_6\text{OR}_1$

**III**  $\begin{matrix} \text{S-(CH}_2\text{)}_6\text{OR}_1 \\ | \\ \text{S-(CH}_2\text{)}_6\text{OH} \end{matrix}$

$\text{R}_1$

a = H

b =  $(\text{iPr})_2\text{NP(OCH}_2\text{CH}_2\text{CN)}$ -

c1 = 5'p(A<sub>20</sub>)-TATCGTTCCATCAGCT [SEQ ID NO: 65]

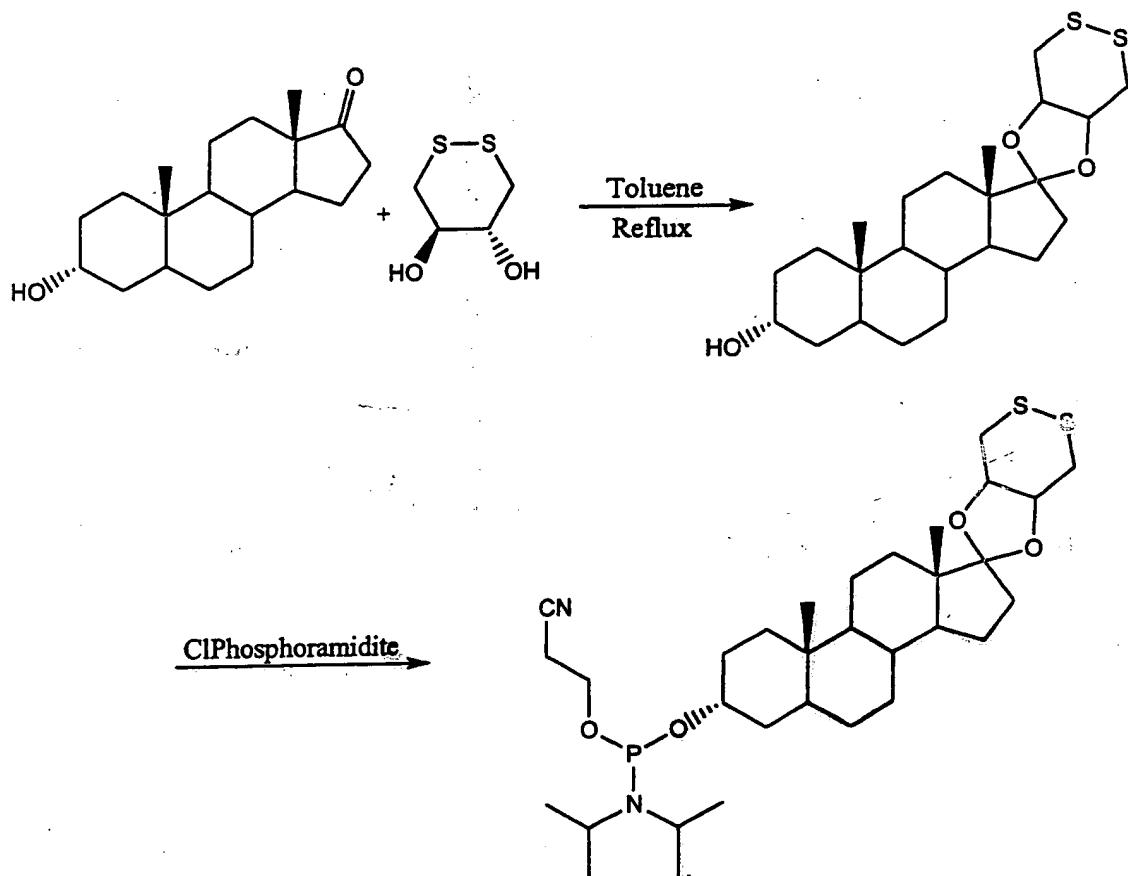
c2 = 5'-p(A<sub>20</sub>)-TTGATCTTCCGTTCT [SEQ ID NO: 66]

Target I = 79-mer oligonucleotide with target region:

3'.....ATAGCAAGGTAGTCGAGCAACTAGAAAGGCAAGA.....5'  
[SEQ ID NO: 67]

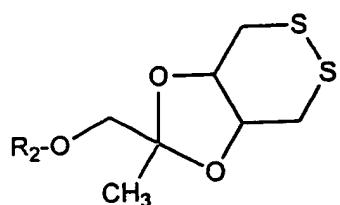
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FIG. 43



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## FIG. 44



R<sub>2</sub>

a = H

b = (iPr)<sub>2</sub>NP(OCH<sub>2</sub>CH<sub>2</sub>CN)-

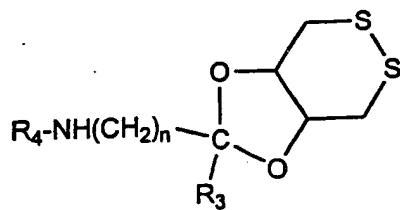
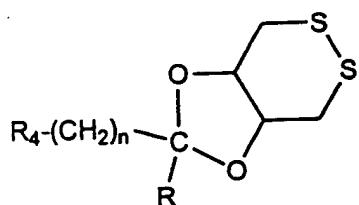
c1 = 5'-p(A<sub>20</sub>)-GCAGACCTCA [SEQ ID NO: 68]

c2 = 5'-p(A<sub>20</sub>)-CCTATGTGTCG [SEQ ID NO: 69]

D = 5'-p(A<sub>20</sub>) [SEQ ID NO: 70]

Target I = 63-mer oligonucleotide with target region:

3'-.....CGTCTGGAGTGGATAACACAGC.....5'  
[SEQ ID NO: 71]



R<sub>3</sub> = hydrogen, an alkyl group, an aryl group, or a substituted alkyl or aryl group

R<sub>4</sub> = an attached oligonucleotide or modified oligonucleotide

## FIG. 45

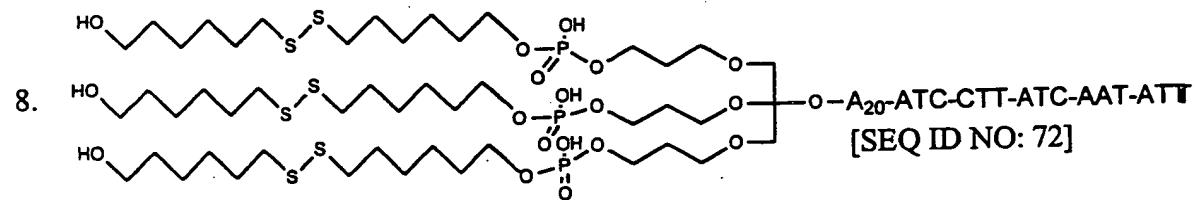
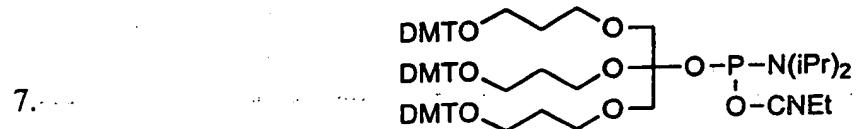
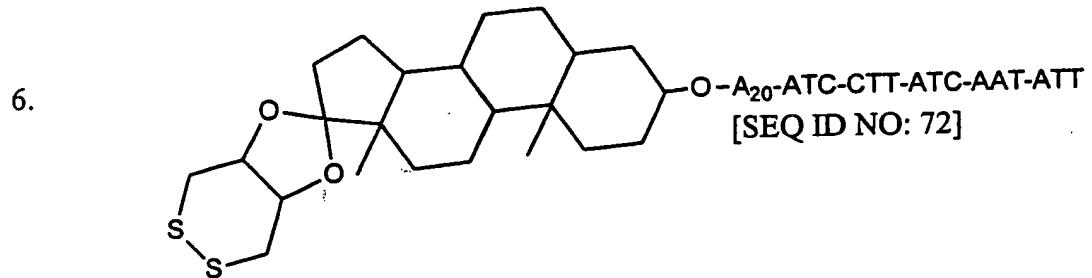
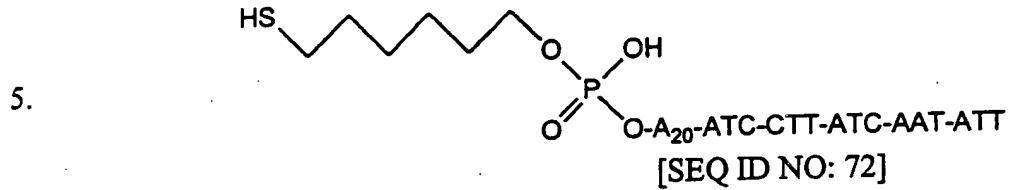
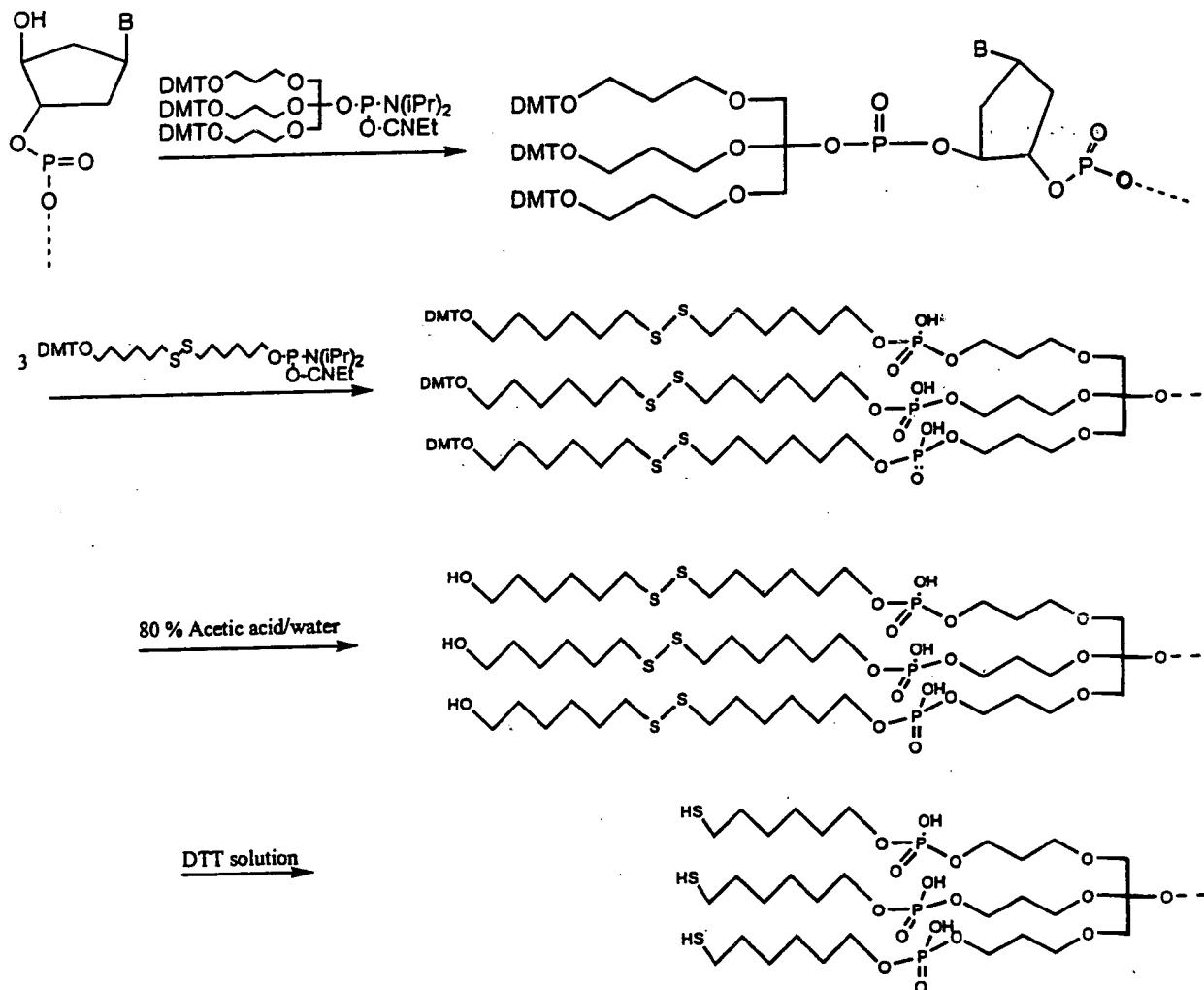


FIG. 46



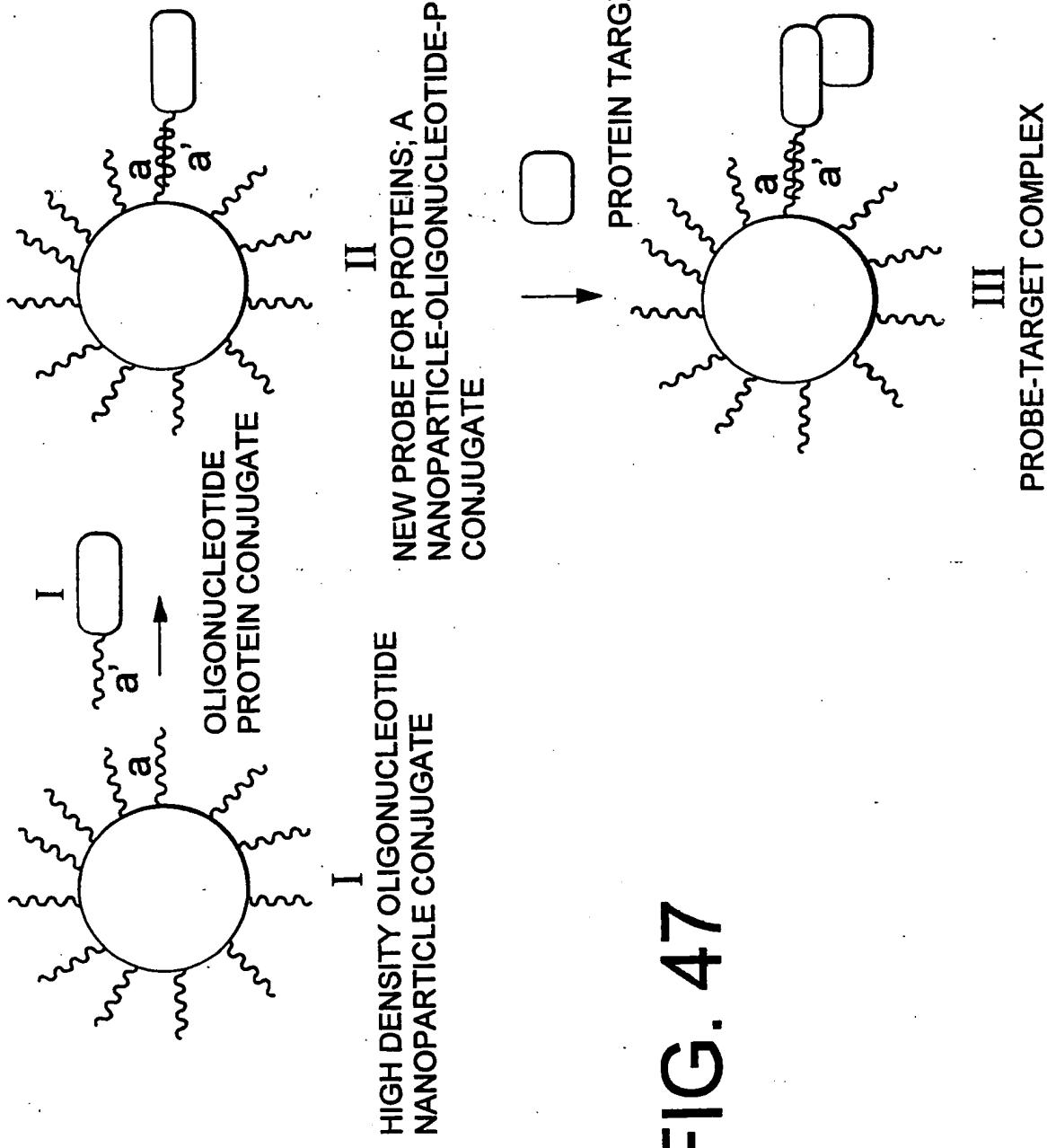
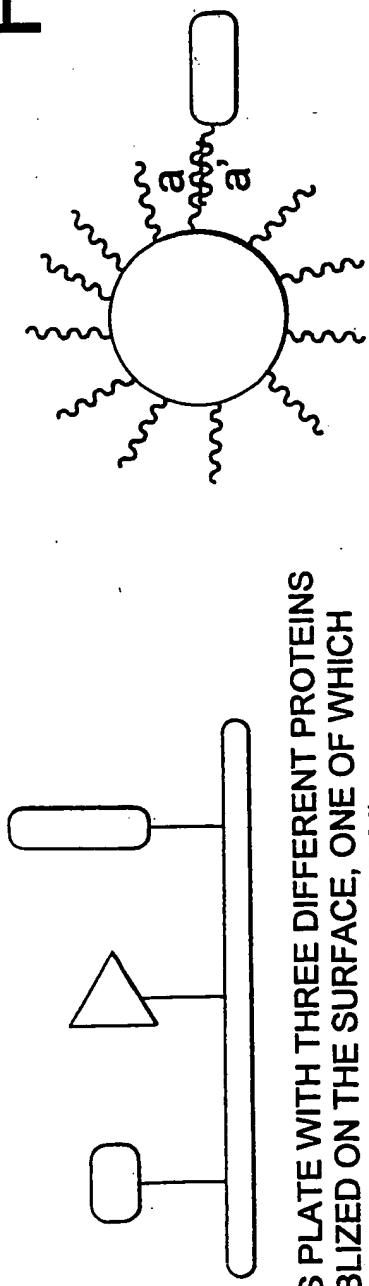


FIG. 47

# FIG. 48

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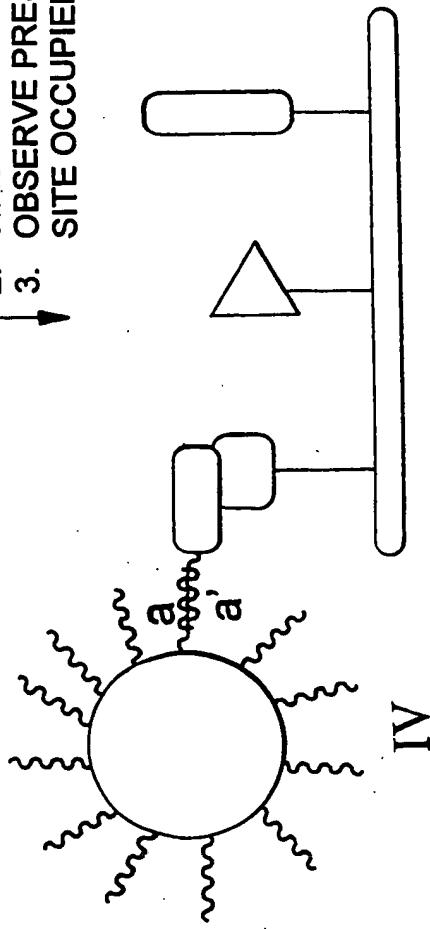


GLASS PLATE WITH THREE DIFFERENT PROTEINS  
IMMOBILIZED ON THE SURFACE, ONE OF WHICH  
BINDS TO THE PROTEIN IN PROBE II

II

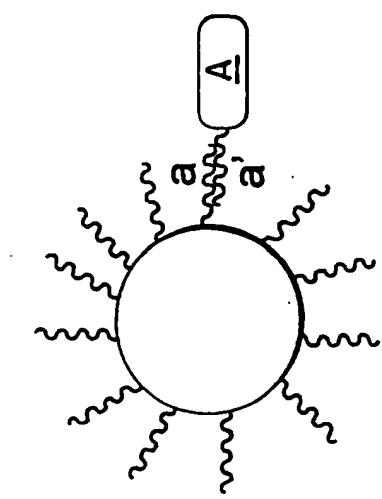
NEW PROBE FOR PROTEINS; A  
NANOPARTICLE-OLIGONUCLEOTIDE-PROTEIN  
CONJUGATE

1. EXPOSE PLATE TO THE PROBE SOLUTION
2. WASH AWAY UNBOUND NANOPARTICLE PROBE
3. OBSERVE PRESENCE OF BOUND NANOPARTICLES AT  
SITE OCCUPIED BY THE FIRST PROTEIN IN THE SERIES.

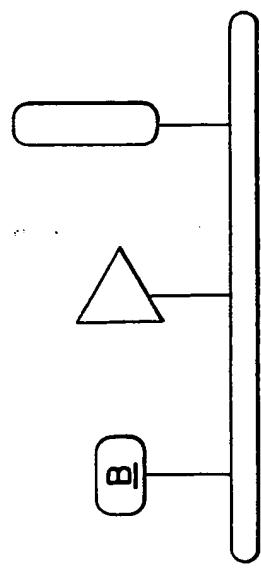


IV

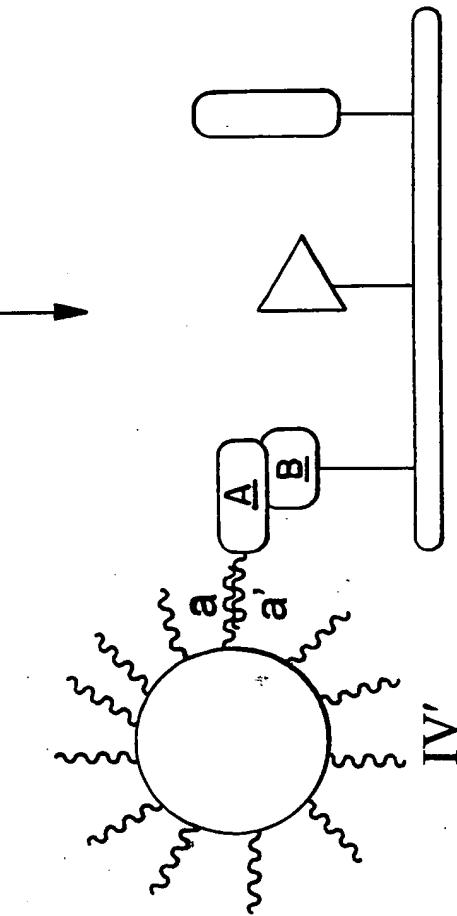
# FIG. 49



II'  
NANOPARTICLE-OLIGONUCLEOTIDE-RECEPTOR

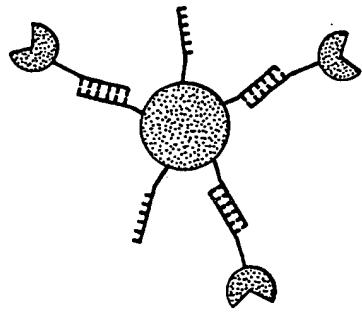


GLASS PLATE WITH THREE DIFFERENT SUBSTANCES  
IMMOBILIZED ON THE SURFACE, ONE OF WHICH (B)  
BINDS TO THE RECEPTOR UNIT (A) IN II'.

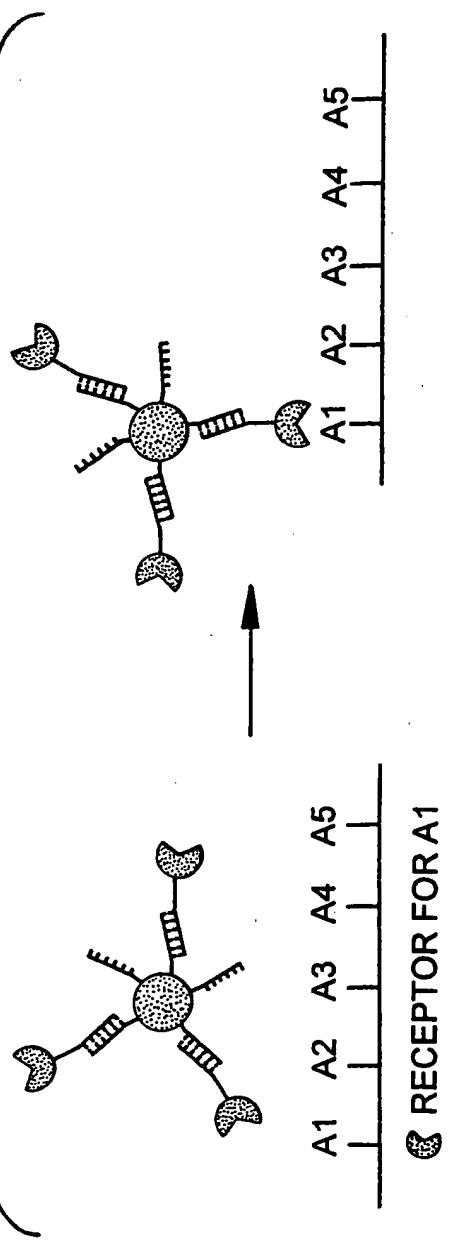


IV'

**FIG. 50A**

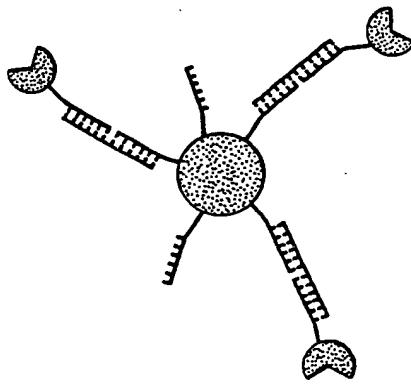


**FIG. 51A**

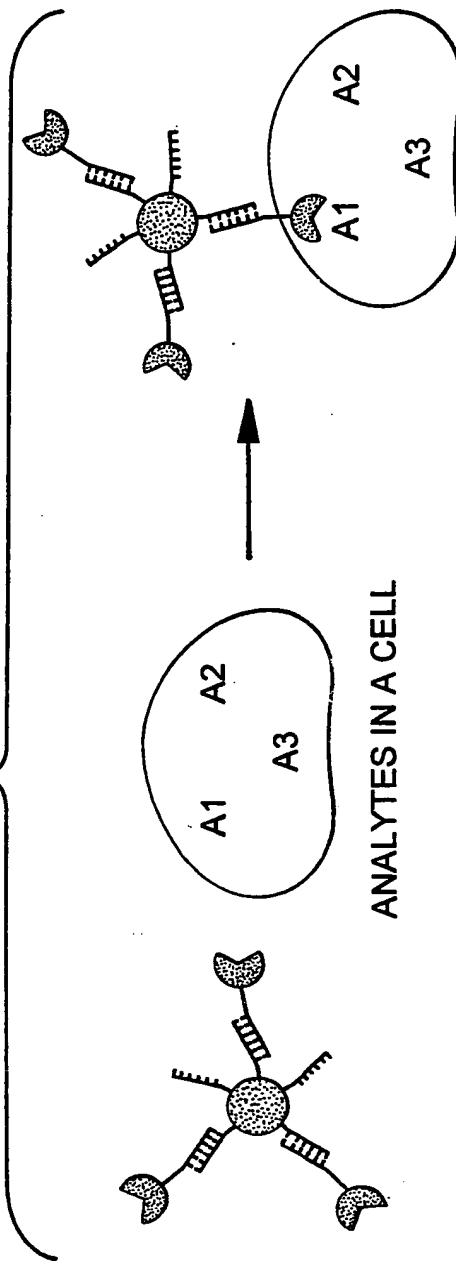


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**FIG. 50B**

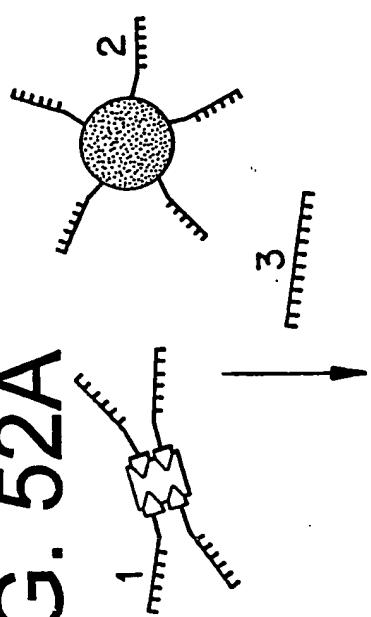


**FIG. 51B**

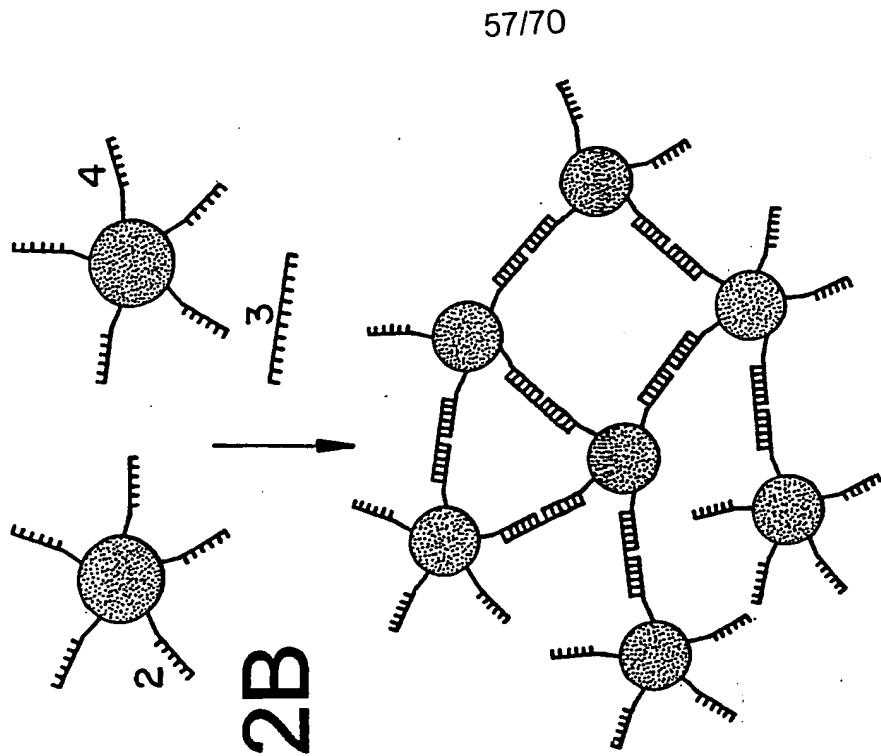


ANALYTES IN A CELL

# FIG. 52A



# FIG. 52B

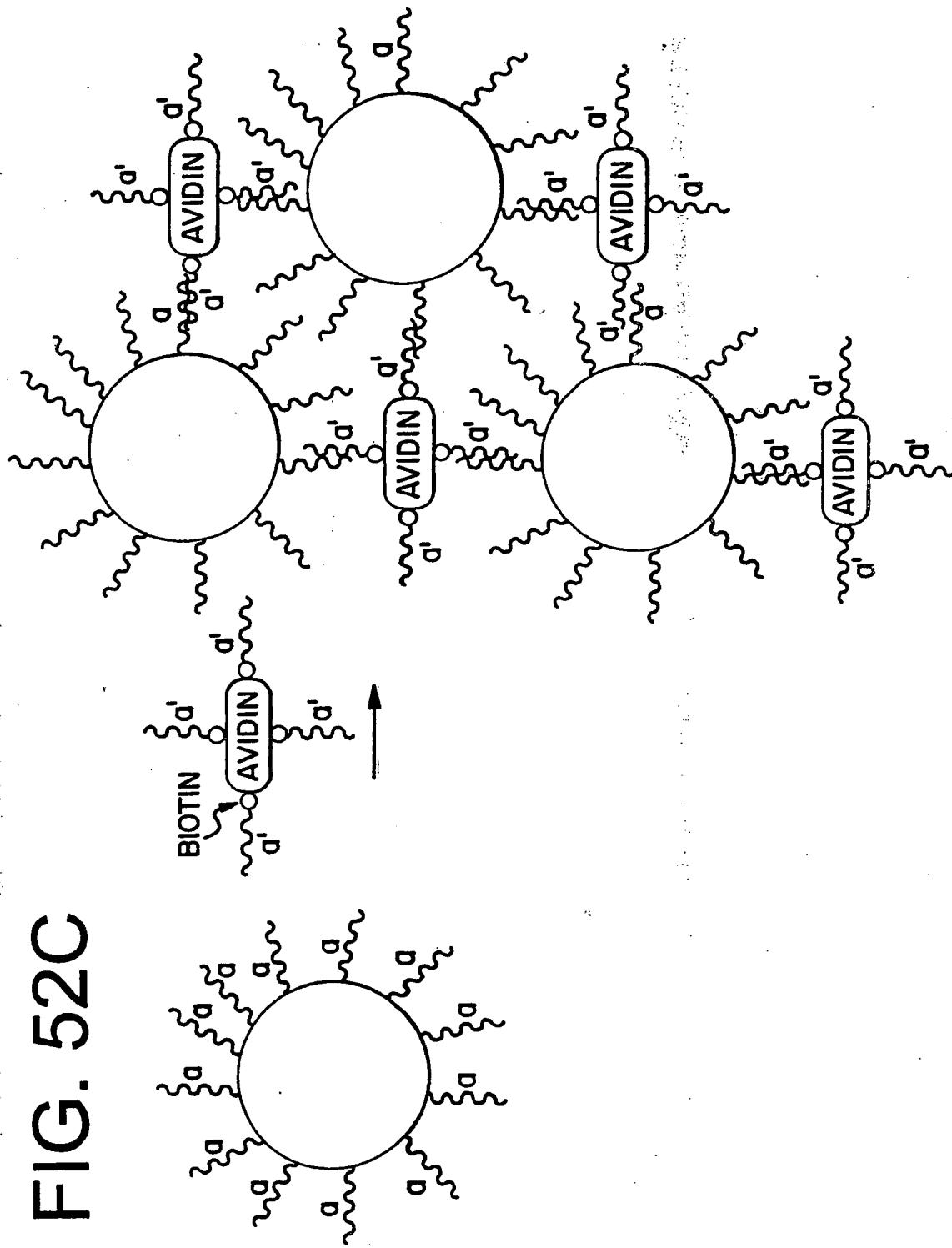


- 1 3' biotin-TEG-A<sub>10</sub>-ATG CTC AAC TCT 5' [SEQ. ID NO. 73]  
2 5' SH(CH<sub>2</sub>)<sub>6</sub>-A<sub>10</sub>-CCG ATT CAG GAT 3'  
3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3'  
4 3' SH(CH<sub>2</sub>)<sub>3</sub>-A<sub>10</sub>-ATG CTC AAC TCT 5'

13 nm Au NANOPARTICLES    [ ] STREPTAVIDIN

13 nm Au NANOPARTICLES

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**FIG. 52C**

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FIG. 53

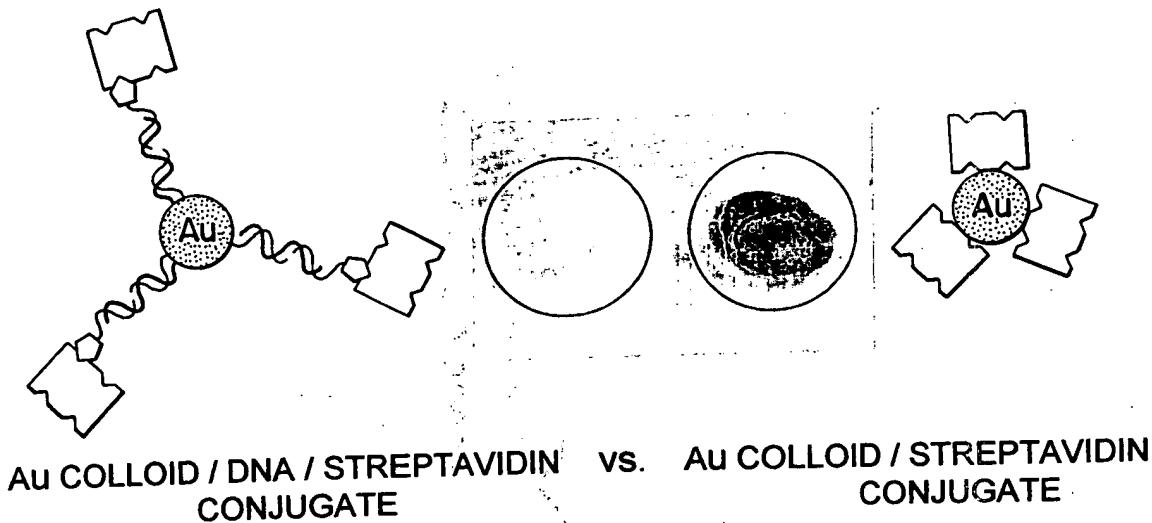
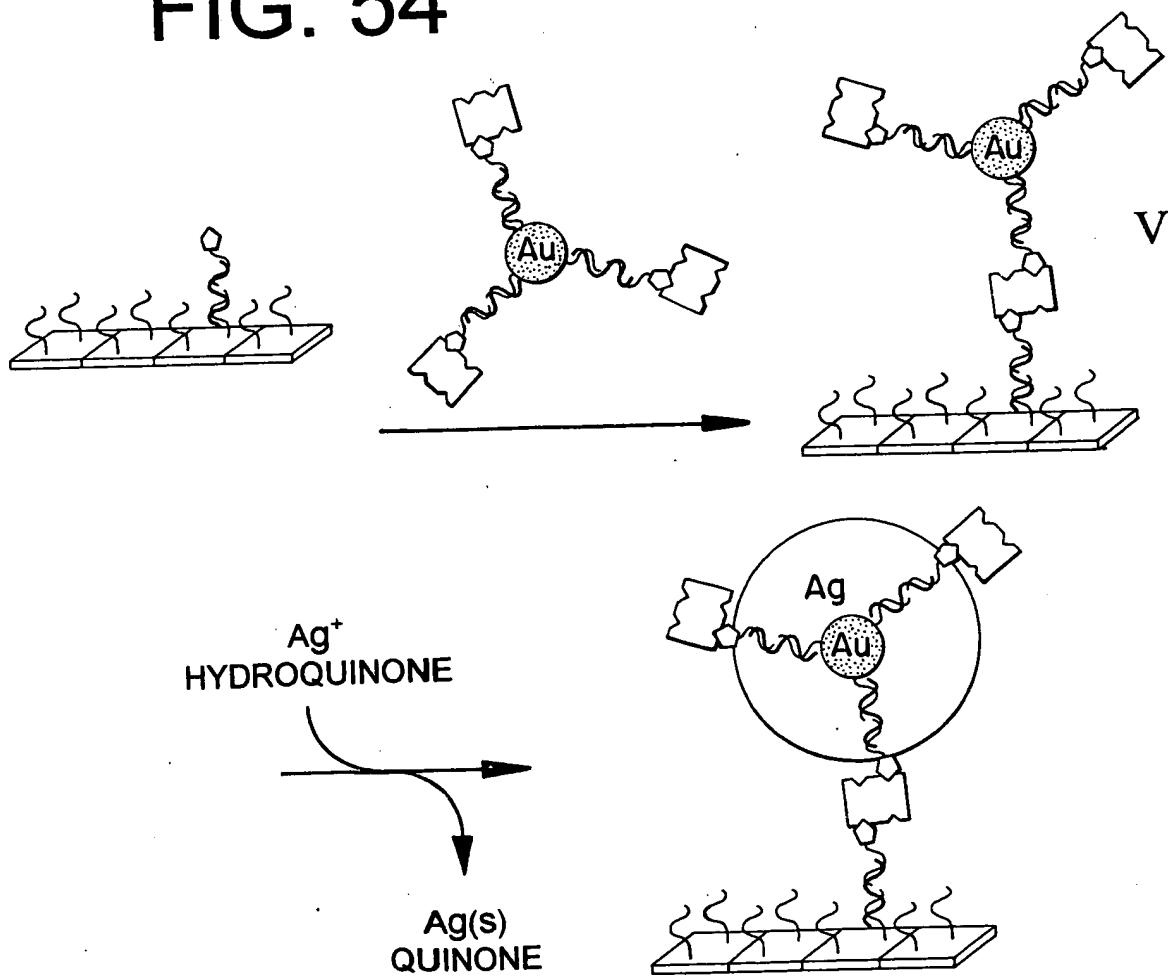
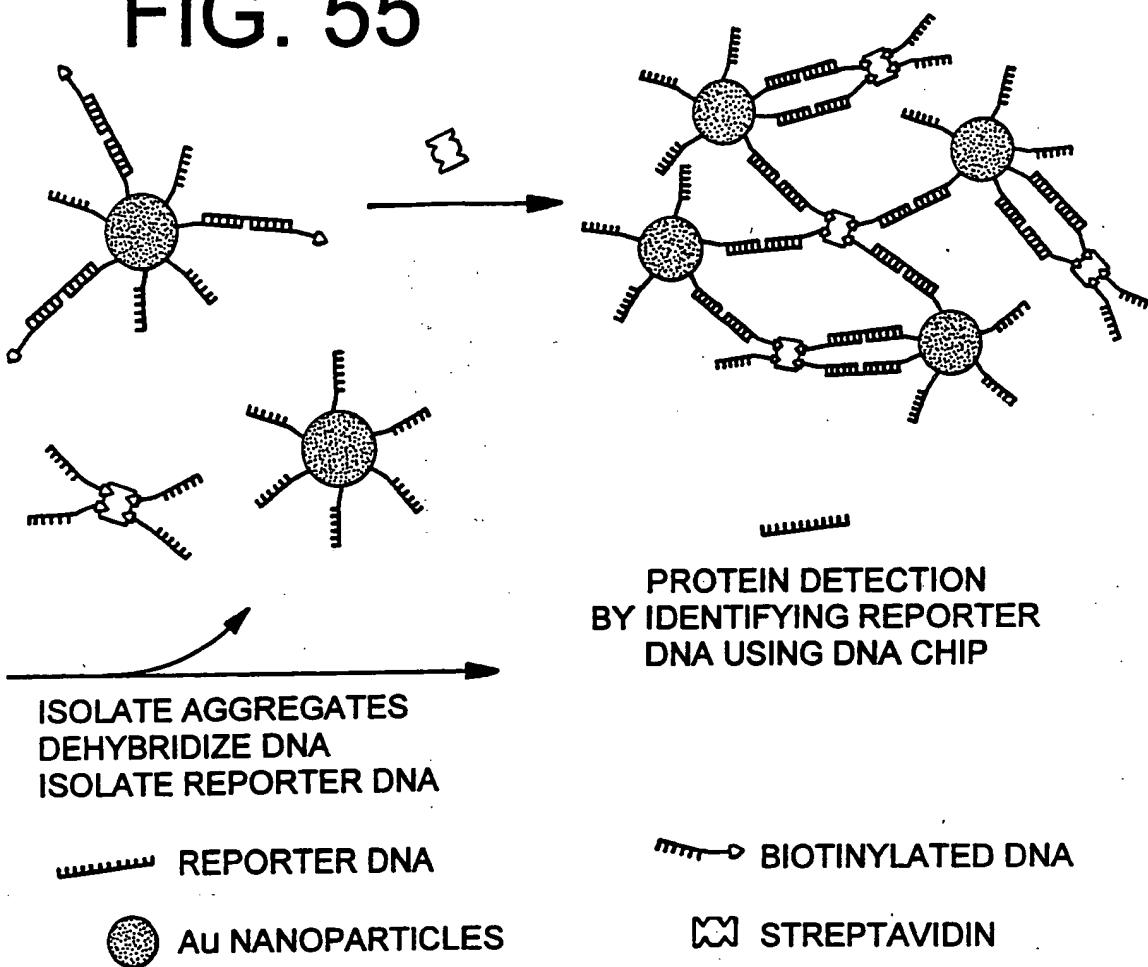


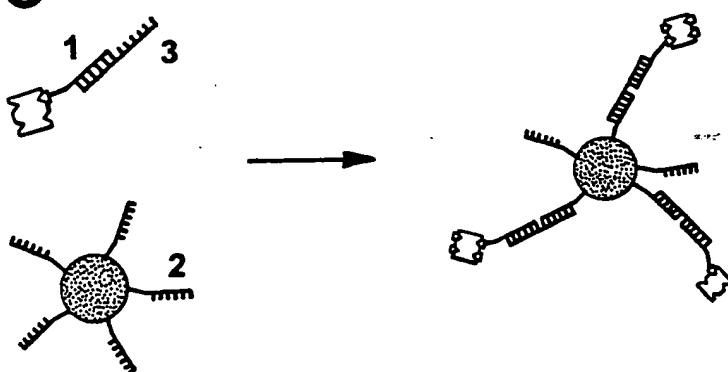
FIG. 54



**FIG. 55** 60/70



**FIG. 56**



- |   |                  |
|---|------------------|
| 1 3' BIOTIN-TEG-A <sub>10</sub> -ATG CTC AAC TCT 5'                         | [SEQ.ID NO: 73]  |
| 2 5' SH(CH <sub>2</sub> ) <sub>6</sub> -A <sub>10</sub> -CGC ATT CAG GAT 3' | [SEQ. ID NO: 74] |
| 3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3'                                     | [SEQ. ID NO: 75] |

13nm Au NANO PARTICLES

STREPTAVIDIN

LINKED DNA

BIOTINYLATED DNA

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FIG.57A

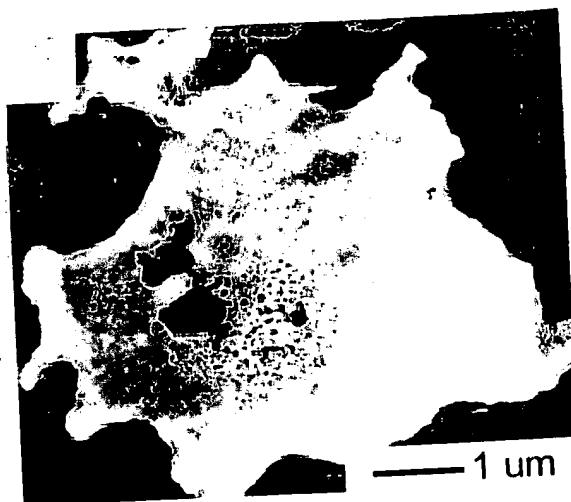
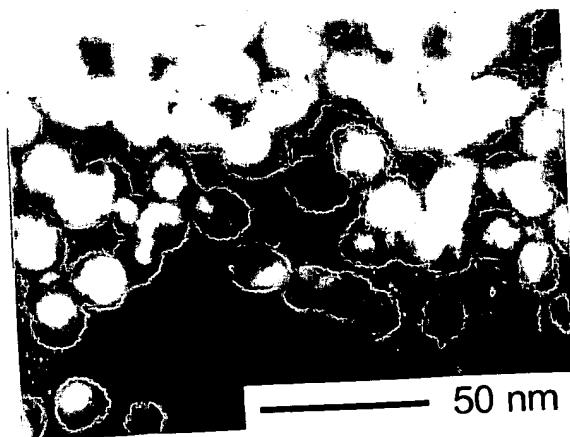
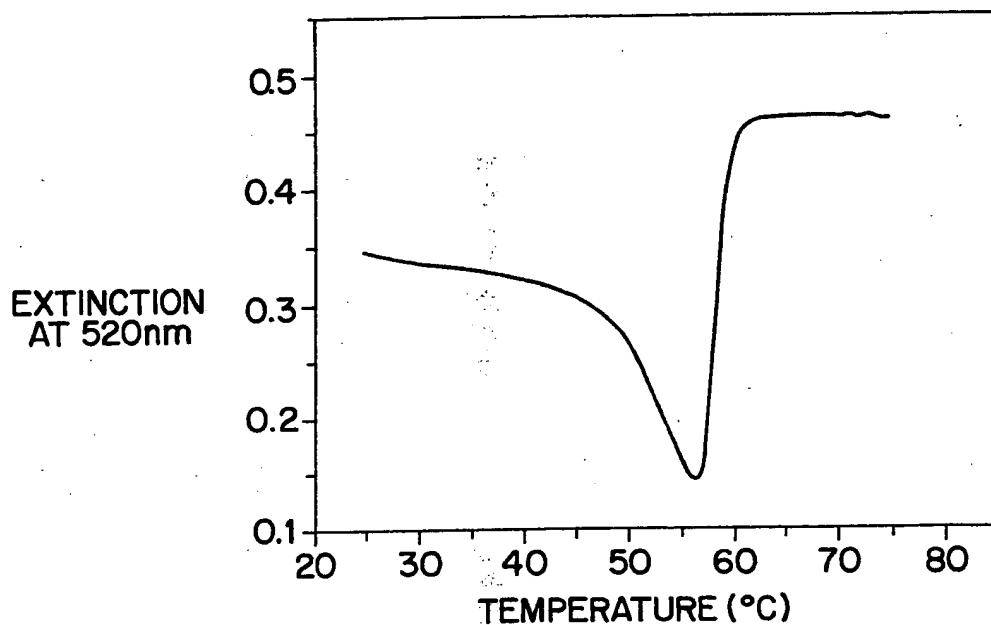


FIG.57B

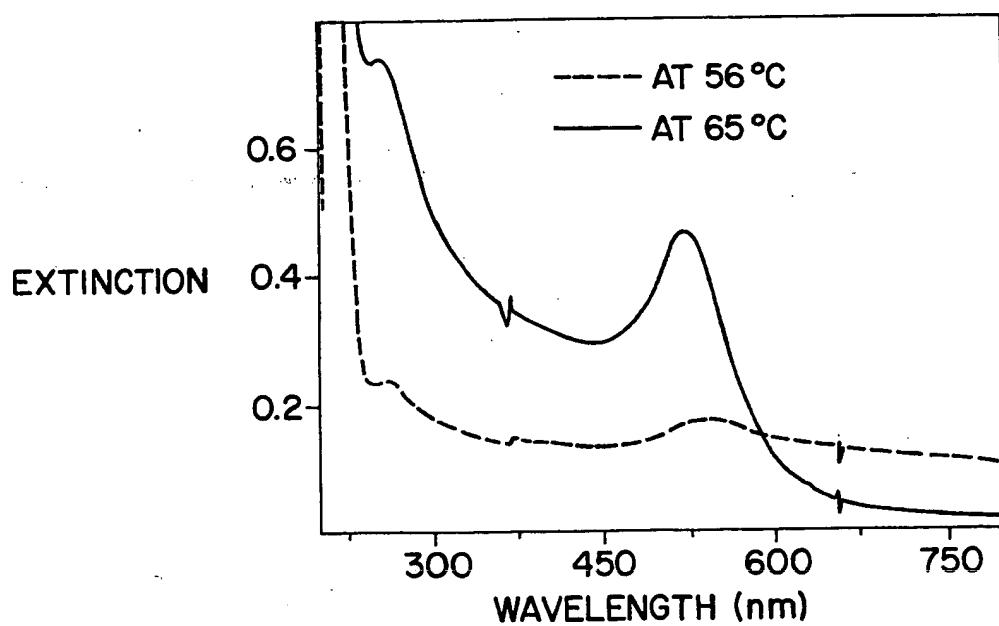


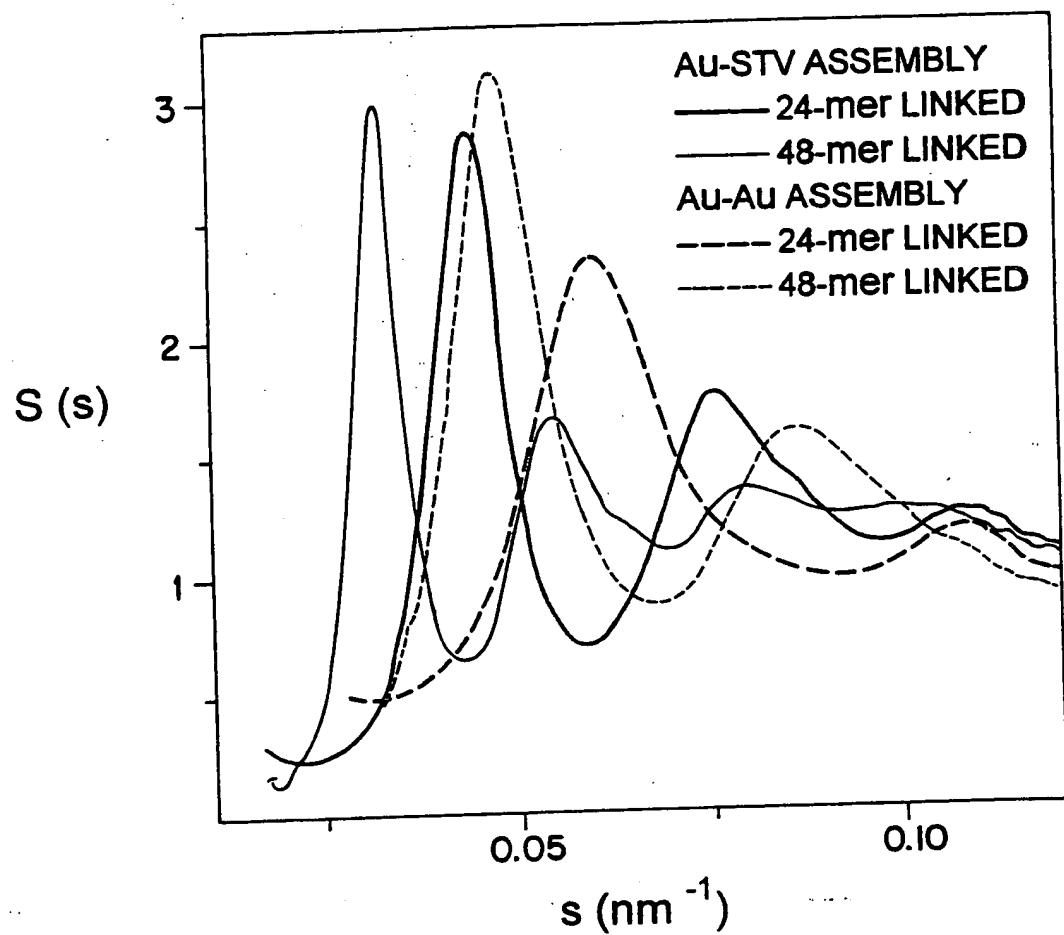
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**FIG. 58A**



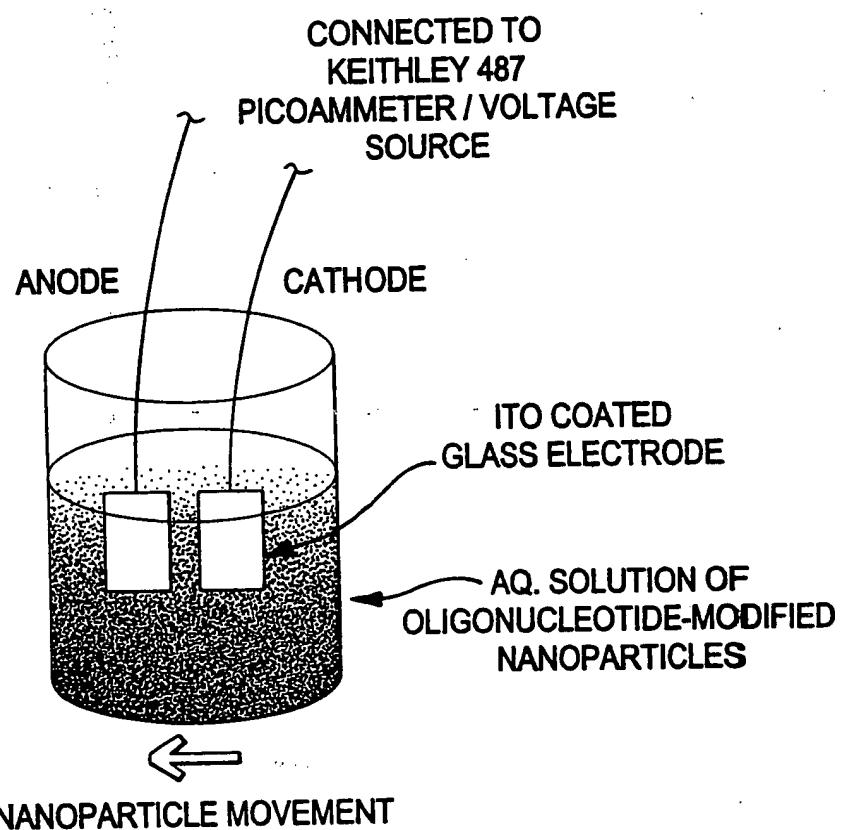
**FIG. 58B**



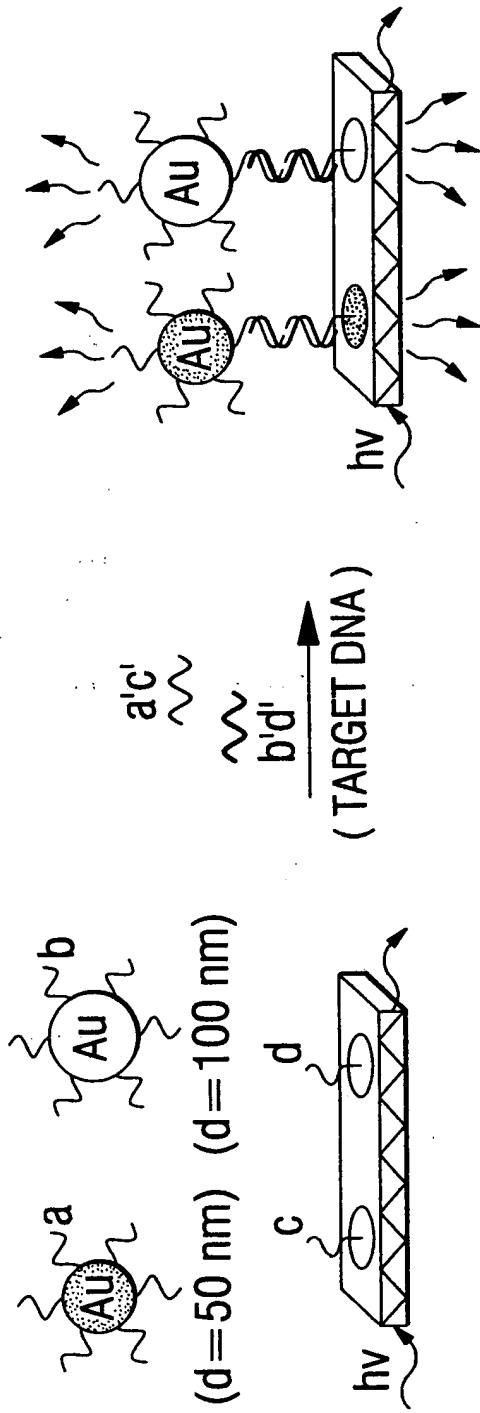
**FIG. 59**

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**FIG. 60**

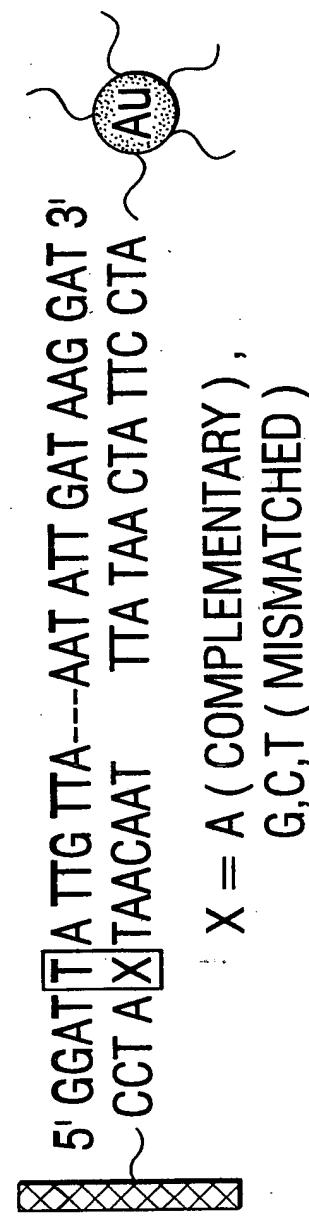


# FIG. 61A



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# FIG. 61B



## FIG. 62

Test for Target  
Sequence *a'c'*

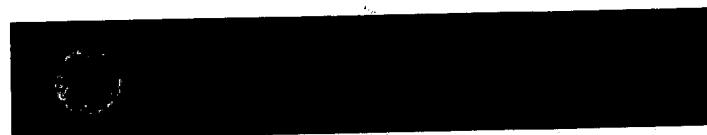
A



B



C



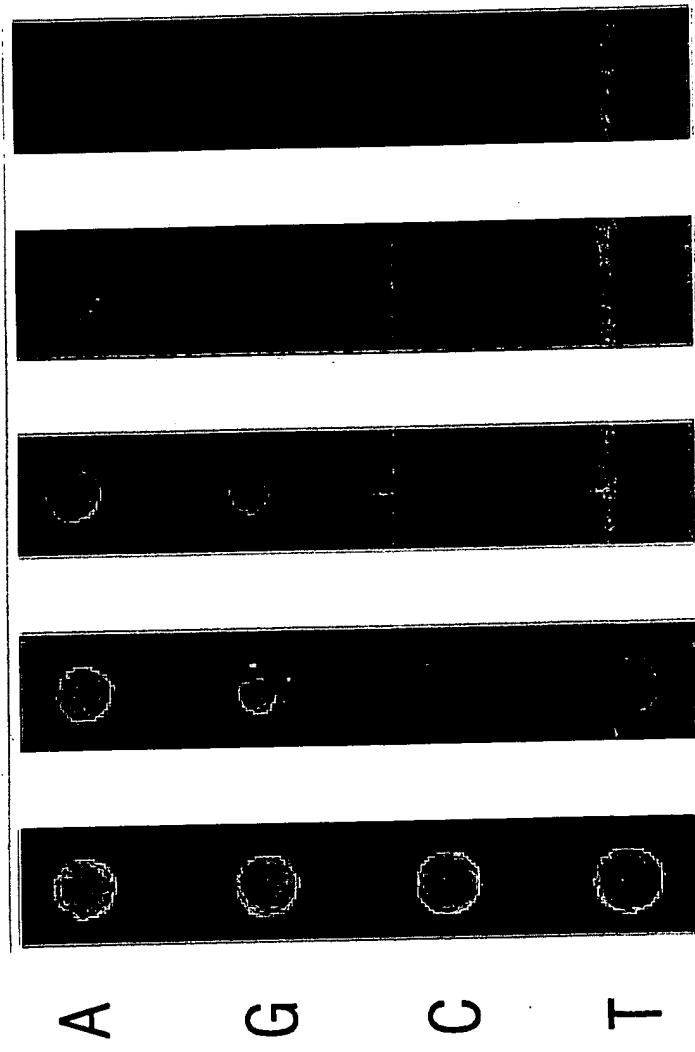
D



Test for Target  
Sequence *b'd'*

**FIG. 63A**

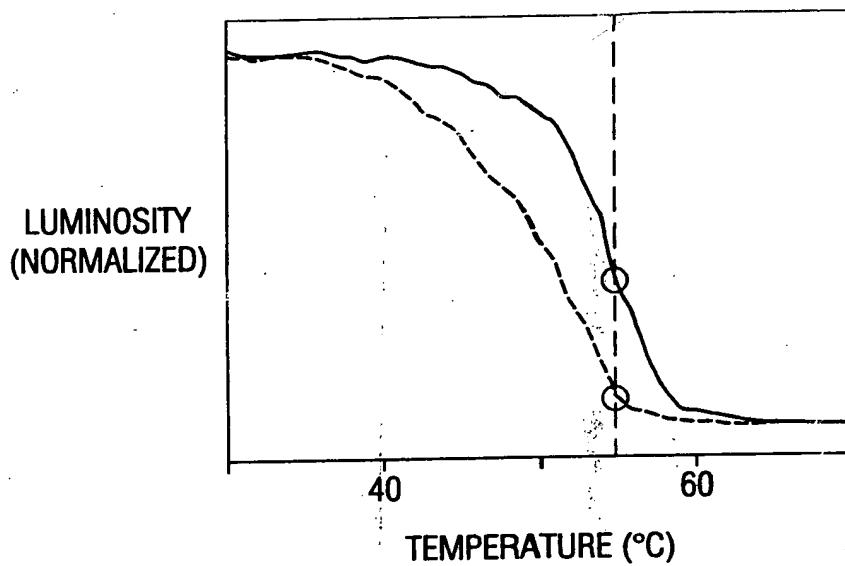
25 °C 49 °C 52 °C 55 °C 59 °C



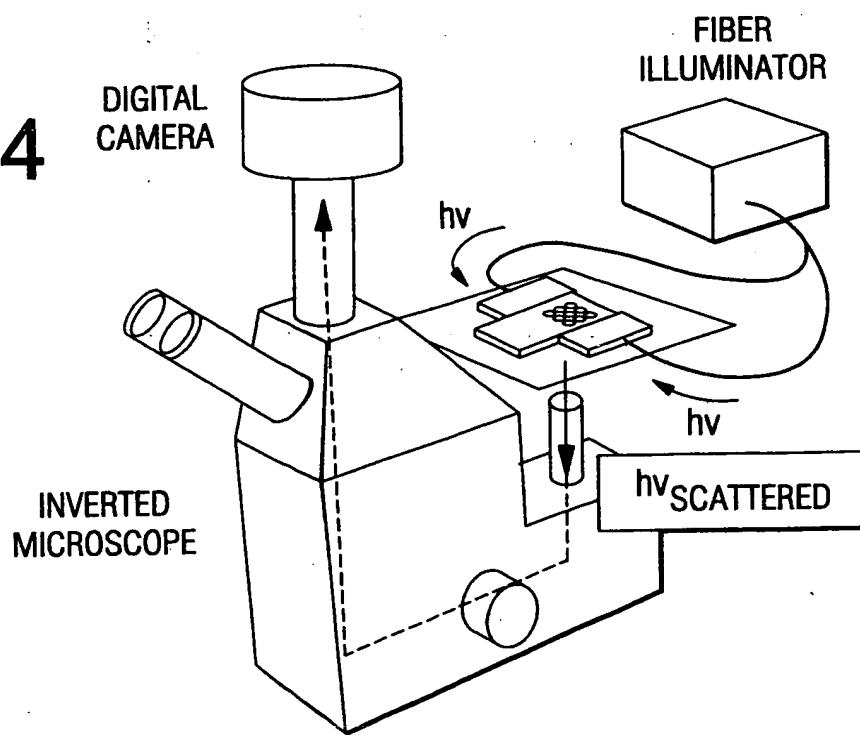
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**FIG. 63B**

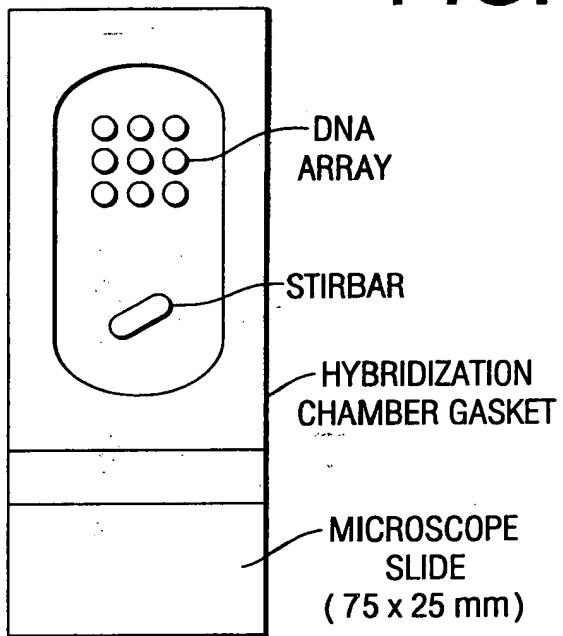


**FIG. 64**

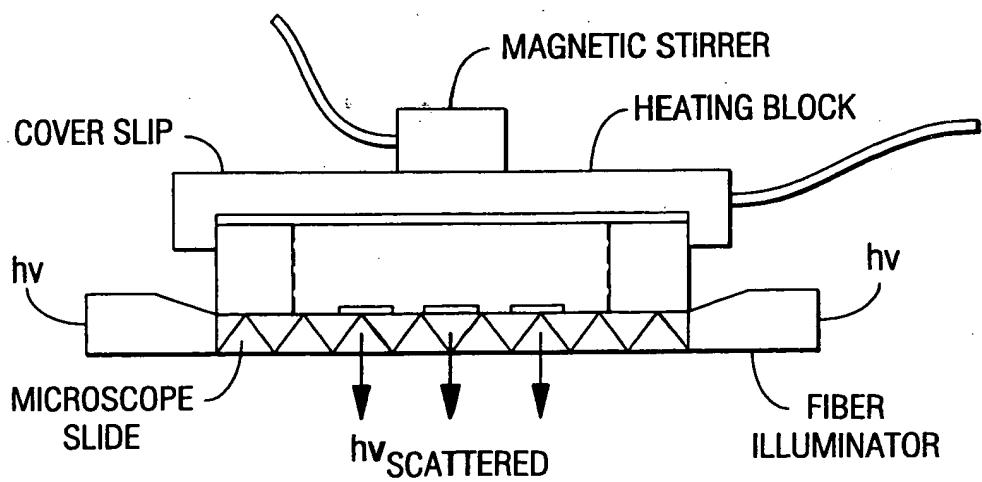


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**FIG. 65A**

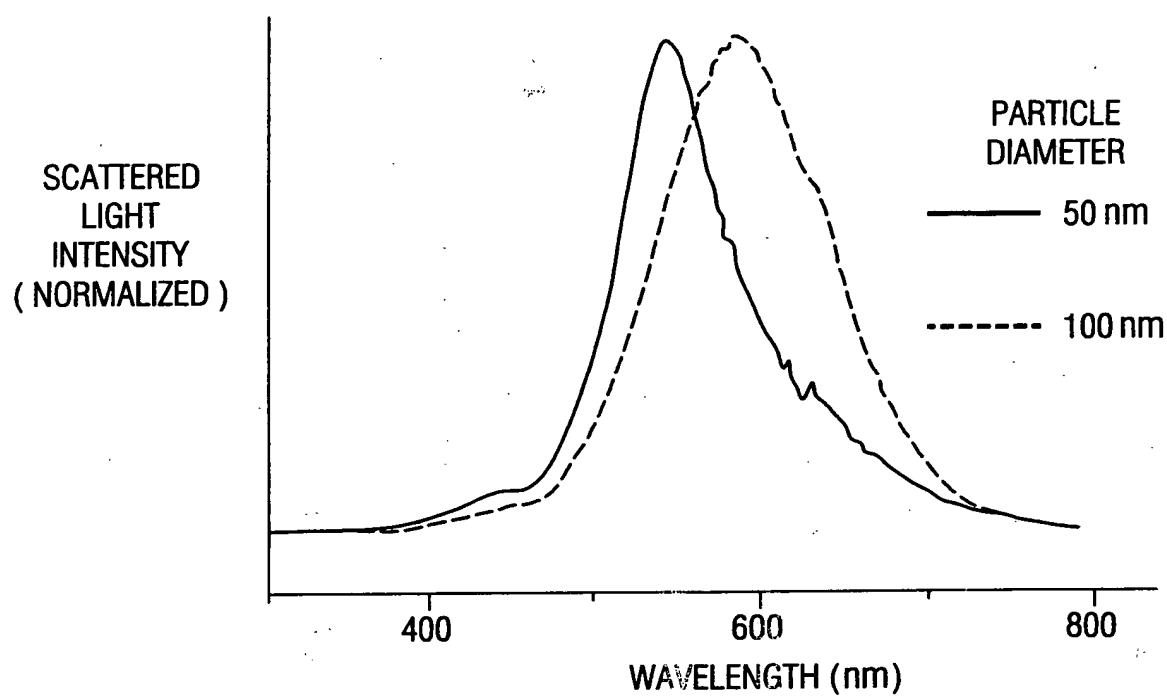


**FIG. 65B**



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**FIG. 66**



**FIG. 67**

